PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE
Vol. 49 No. 8 August 1956

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Section of Epidemiology and Preventive Medicine

President—MAURICE MITMAN, M.D., F.R.C.P., D.P.H.

[*April* 20, 1956]

Patients in Mental Hospitals

By W. P. D. LOGAN, M.D., Ph.D., D.P.H.

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IT is not my purpose in this paper to attempt any comprehensive review of the epidemiology of mental disease but to put before you some illustrative material derived from the scheme operated by the General Register Office for the compilation of statistics of patients in mental hospitals. This scheme began in 1949 and covers all National Health Service mental hospitals and mental deficiency hospitals. A return is submitted to the General Register Office in respect of each admission and each discharge to these hospitals and annual statistics of admissions and discharges are published. In addition estimates are made of numbers of patients resident in the hospitals at the end of each year, and these estimates have been supplemented by two special censuses of patients resident in the hospitals on December 31, 1949, and on December 31, 1954. Recently the scheme was amplified by the introduction of a continuous central index of patients admitted for the first time on or after January 1, 1954, provision being made for the "longitudinal" recording of subsequent readmissions of each patient to the same or any other mental hospital in the scheme.

Number of patients in mental hospitals.—At the national population census on April 8, 1951, 417,000 patients were enumerated in National Health Service hospitals in England and Wales, and of these, 191,000 or 46% were patients in mental and mental deficiency hospitals (Table I). This paper will deal only with patients in mental hospitals (141,000 or 34%), though corresponding statistics are now available for mental deficiency hospitals.

The average number of patients in mental hospitals in 1869 was about 35,000. This increased gradually over the years to 140,000 in 1939 (Table II), followed by a decline

TABLE I.—PATIENTS IN N.H.S. HOSPITALS ON CENSUS NIGHT, APRIL 8, 1951. ENGLAND AND WALES

Type of hospital	No. of patients	Per cent
Teaching ..	22,000	*5*
Non-teaching ..	204,000	*49*
Mental	141,000	*34*
Mental deficiency	50,000	*12*
Total	417,000	*100*

TABLE II.—DAILY AVERAGE NUMBER OF PATIENTS IN MENTAL HOSPITALS AND NUMBER OF ANNUAL ADMISSIONS. SELECTED YEARS. ENGLAND AND WALES

Year	Daily average number of patients	Annual admissions
1869	35,000	10,000
1899	82,000	19,000
1929	122,000	22,000
1939	140,000	32,000
1948	136,000	51,000

during the 1939–45 war and the immediate post-war years. Annual *admissions* were less retarded by the war and numbered 51,000 in 1948 compared with 32,000 in 1939.

The trend during the recent "National Health Service" period is given in Table III. Numbers of patients resident have increased a little, and numbers of annual admissions have increased a lot—by 11,000 (24%) since 1950 at ages under 65, and by 4,000 (40%) at ages 65 and over. Concurrently the proportion of readmissions has gone up from 33 to 40%.

TABLE III.—NUMBER OF PATIENTS IN N.H.S. MENTAL HOSPITALS ON DECEMBER 31 OF EACH YEAR, AND NUMBER OF ANNUAL ADMISSIONS, 1950 TO 1954. ENGLAND AND WALES

	No. of patients resident	Admissions			Per cent readmissions
		Under 65	65+	All ages	
1950 ..	142,000	46,000	10,000	56,000	*33*
1951 ..	143,000	47,000	12,000	59,000	*35*
1952 ..	145,000	50,000	12,000	62,000	*37*
1953 ..	147,000	54,000	13,000	67,000	*37*
1954 ..	148,000	57,000	14,000	71,000	*40*

Sex and age distribution.—41% of the 59,000 patients admitted in 1951 were males, less than half of them aged under 45, and a fifth aged over 65 (Table IV). Females predominated at all ages from 25 upwards. The female admission rates increased steadily with age whereas the male rates were diminished between 35 and 54. In contrast to admissions the maximum number of male patients resident was at ages 45–54 but for females it was at ages 65 and over.

TABLE IV.—MENTAL HOSPITALS. NUMBER OF PATIENTS ADMITTED DURING 1951 AND ESTIMATED NUMBER OF PATIENTS RESIDENT ON DECEMBER 31, 1951

Rates per 100,000 population

Direct admissions		0–	16–	20–	25–	35–	45–	55–	65+	All ages
No.	M	306	711	1,897	5,152	4,356	3,964	3,502	4,524	24,412
	F	212	811	1,870	5,526	6,498	6,685	5,645	7,629	34,876
Rate	M	6	85	154	169	133	137	171	230	119
	F	4	74	127	172	191	214	222	268	153
Residents										
No.	M	211	440	1,581	7,704	11,678	13,907	12,322	12,918	60,761
	F	149	388	1,313	6,015	11,447	16,948	18,950	27,225	82,435
Rate	M	4	53	128	253	357	482	603	656	296
	F	3	35	89	188	337	543	744	957	363

Voluntary, temporary and certified patients.—Just over two-thirds of male admissions and just under two-thirds of female admissions were voluntary (Table V). There were

TABLE V.—STATUS OF PATIENTS ADMITTED TO MENTAL HOSPITALS, 1951

	M	% first admission	F	% first admission
Voluntary	16,607	*66*	22,107	*64*
Temporary	449	*85*	825	*85*
Certified	7,356	*66*	11,944	*65*

only a few hundred patients admitted as temporary patients, twice as many female as male, and 85% were first admissions. The proportion of voluntary admissions was between 65 and 80% at ages up to 65, thereafter falling abruptly (Table VI).

TABLE VI.—MENTAL HOSPITALS. PERCENTAGE OF VOLUNTARY ADMISSIONS BY SEX AND AGE, 1951

	0–	20–	25–	35–	45–	55–	65–	75+	All ages
M	79	69	72	73	77	70	53	35	68
F	78	71	72	70	69	65	51	26	63

Regional variations.—The admission rates (males) into hospitals in the various hospital regions are given in the map diagram (Fig. 1), and show a range of rates from 144 in the South Western to 89 in the Manchester region. Much of this variation is probably due to differences between the regions in their admission policy.

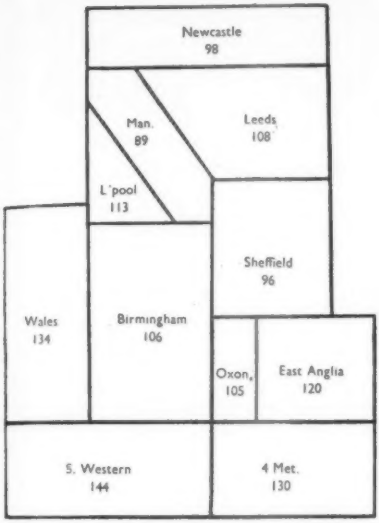

FIG. 1.—Mental Hospitals. Admission rates per 100,000 population by Regional Hospital Board areas. Males, 1951.

TABLE VII.—MENTAL HOSPITALS. PERCENTAGE DISTRIBUTION OF ADMISSIONS BY DIAGNOSTIC GROUPS. 1951

	M	F
Psychoses	65	73
Psychoneuroses	16	16
Behaviour, character and intelligence disorders	8	3
Others	11	8
Total	100	100

Diagnoses.—The broad distribution of diagnoses into four main categories is given in Table VII. Two-thirds of male, almost three-quarters of female admissions were on account of psychoses. The psychoses admission rates of females were considerably higher than of males due to their excess rates for manic-depressive reaction (Table VIII). Amongst the psychoneuroses anxiety reaction caused equal admission rates for the two sexes, but the other psychoneuroses gave a female excess. Males on the other hand had higher admission rates for pathologic personality, behaviour disorders, consequences of syphilis and epilepsy.

TABLE VIII.—MENTAL HOSPITALS. DIRECT ADMISSIONS PER MILLION POPULATION, BY DIAGNOSIS. 1951

(International Statistical Classification Numbers in Brackets)

	M	F
Schizophrenia (300)	271	254
Manic-depressive reaction (301)	258	486
Senile Psychosis (304)	114	192
Psychoses, all forms except puerperal (300–309)	*757*	*1,121*
Anxiety reaction (310)	81	81
Hysterical reaction (311)	26	54
Neurotic depressive reaction (314)	42	73
Psychoneuroses, all forms (310–318)	*181*	*242*
Pathologic personality (320)	52	22
Mental deficiency (325)	19	18
Behaviour, character and intelligence disorders, all forms (320–326)	*92*	*51*
Syphilis (020–029)	15	7
Epilepsy (353)	40	32

There were very striking differences in regional admission rates for some of these diagnoses (Table IX). For example, at certain ages the Liverpool hospital region had high

TABLE IX.—MENTAL HOSPITALS. SELECTED REGIONAL ADMISSION RATES PER MILLION. 1951

Diagnosis	Sex	Age	Region	Rate	Region	Rate
Schizophrenia ..	M	20–24	Liverpool	1,054	Oxford	463
Manic-depressive	F	65–74	S.W.	1,030	Liverpool	323
Anxiety reaction	M	25–34	Liverpool	375	Sheffield	95
Epilepsy	F	20–24	Liverpool	127	Newcastle	10

rates for schizophrenia, anxiety reaction and epilepsy, and the lowest rate for manic-depressive reaction. It is unlikely that these differences have much real epidemiological significance.

Place of residence.—Admission rates (all diagnoses) (Table X) were highest for residents of County Boroughs and lowest for Rural Districts. For schizophrenia and behaviour disorders, however, Greater London had the highest rate.

TABLE X.—MENTAL HOSPITALS. ADMISSIONS PER 100,000 MALES, BY PLACE OF RESIDENCE. 1951

	Greater London	County Boroughs	Urban Districts	Rural Districts
Schizophrenia	32	29	24	18
Manic-depressive reaction	24	27	26	22
Psychoneuroses	18	20	19	12
Behaviour, character and intelligence disorders..	10	9	9	6
All diagnoses	118	127	111	85

Religious affiliation.—The distribution of diagnoses of male patients admitted in 1950, according to religion, is shown in Table XI. No important differences are discernible other than a high proportion (30%) of admissions on account of disorders of character, behaviour and intelligence amongst patients stated to have no religion.

TABLE XI.—MENTAL HOSPITALS. PERCENTAGE DISTRIBUTION OF MALE ADMISSIONS BY RELIGION AND TYPE OF DISEASE. 1950

	Psychoses	Psycho-neuroses	Behaviour disorders	Others	Total	Number
Church of England	65	15	8	12	100	16,917
Roman Catholic..	66	15	9	10	100	2,665
Nonconformist ..	68	15	6	11	100	3,054
Jewish	71	11	9	9	100	280
Others	69	14	7	10	100	524
None	47	18	30	5	100	130
Not known ..	69	11	10	10	100	300
Total	65	15	8	12	100	23,870

Marital status.—Two ages have been selected in Table XII to illustrate differences in admission rates between single patients and married, widowed and divorced. Rates were in each instance higher among the single, but generally less so in the higher age group, where in many instances the marital status would be determined before the onset of mental disease, than in the younger group in whom the mental disease would often constitute an impediment to marriage. Table XII incidentally shows the very large differences there are in the admission rates, especially for schizophrenia, between the younger and the older group.

TABLE XII.—MENTAL HOSPITALS. ADMISSION RATES PER MILLION POPULATION AT AGES 25–34 AND 55–64 BY SEX, MARITAL STATUS, AND DIAGNOSIS. 1950

		25–34		55–64	
		M	F	M	F
Schizophrenia	Single	2,024	1,617	219	206
	M W D	230	296	43	104
Manic-depressive reaction	Single	360	534	953	1,331
	M W D	139	372	666	919
All neuroses	Single	471	622	231	273
	M W D	256	420	180	216
Epilepsy	Single	191	176	124	36
	M W D	29	29	29	18
Disorders of character, behaviour and intelligence	Single	380	282	189	64
	M W D	94	45	39	9
All diagnoses	Single	3,800	3,400	2,900	2,800
	M W D	800	1,300	1,600	1,900

Social class.—Age-standardized ratios of male admissions according to diagnosis and the Registrar General's five social classes (Table XIII) indicate a very clear-cut tendency

TABLE XIII.—MENTAL HOSPITALS. STANDARDIZED ADMISSION RATIOS BY SOCIAL CLASS AND DIAGNOSIS. MALES. 1951

	I	II	III	IV	V
Schizophrenia	70	67	85	94	216
Manic-depressive reaction	103	83	90	99	163
Senile psychosis	73	69	87	93	204
Alcoholic psychosis	155	222	65	58	141
Psychosis, all forms	*82*	*75*	*86*	*96*	*195*
Anxiety reaction	67	72	104	80	152
Hysterical reaction	64	72	100	89	157
Psychoneuroses	*73*	*72*	*101*	*86*	*152*
Alcoholism	467	173	66	49	127
Mental deficiency	91	52	37	156	347
Behaviour, character and intelligence disorders	*188*	*79*	*79*	*84*	*209*
Epilepsy	30	63	62	109	305
Others	73	67	93	84	195
All diagnoses	*85*	*74*	*88*	*93*	*192*

for high admission rates in Social Class V (unskilled occupations) compared with the others. Notable exceptions were the admissions on account of alcoholic psychosis and alcoholism where Social Classes I and II (professional and managerial occupations) were in the lead; alcoholism is classed in the group of behaviour disorders and so explains the high ratio for Social Class I for this group as a whole.

It is an obvious qualification to most of the diagnoses, that the mental disorder may often have determined the social class of the patient rather than the reverse. In the case of alcoholism, however, it is hardly probable that a taste for excessive drinking will have elevated many patients to Social Classes I and II; rather they are the victims of their comfortable circumstances, though some of the excess may be due to a greater willingness on the part of Social Class I and II patients to seek treatment for their disability than in the other Social Classes.

For most of the mental disorders the social class gradients shown in Table XIII were reproduced at each age group. An exception was manic-depressive reaction where there was a reversal of the social gradient at ages over 65 and a very much higher admission rate of patients in Social Class I than in the other four classes (Table XIV).

TABLE XIV.—MENTAL HOSPITALS. ADMISSION RATES PER MILLION MALES AT AGES 25–34 AND 65+. MANIC-DEPRESSIVE REACTION

	I	II	III	IV	V
Ages 25–34	82	143	154	191	318
Ages 65+	684	421	425	331	346

Conclusion.—In this survey of mental hospital patients I have omitted reference to many other data available from the General Register Office scheme, notably statistics of hospital discharges and of the long-stay patients; and I have not dealt with patients in mental deficiency hospitals. From the point of view of epidemiological research into mental disorder it is necessary always to remember the very serious and well-known deficiencies of hospital statistics because of the various selective factors that decide which patients shall go into hospital and into which hospitals they shall go. However, although much of the value of the kind of mental hospital statistics that we are producing will be administrative rather than epidemiological, I believe that they can and will serve as important foundations for future research, by more refined and more narrowly aimed methods, into the distribution of the mental disorders and the factors that determine this distribution. In particular I have great hopes for the longitudinal type of approach embarked upon in the form of a continuous central index of readmissions. Provided the volume of work associated with this venture does not prove too much for us I believe we shall before very long begin to get a much more informative statistical picture of the patients that go into mental hospitals and of what their long-term prognosis is likely to be.

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Section of Surgery

President—JOHN BRUCE, C.B.E., T.D., F.R.C.S.Ed.

[*January* 4, 1956]

DISCUSSION ON THE SURGICAL MANAGEMENT OF UNCOMPLICATED DUODENAL ULCER

Mr. R. L. Holt:

The objectives of the surgical treatment of duodenal ulcer are essentially twofold—the cure of the original ulcer, and the avoidance of subsequent digestive disturbances. May I point out gently in passing that many surgeons appear to have concentrated so much on the first objective that they have tended to overlook the second.

Since Dragstedt's reintroduction of vagotomy in 1943 (Dragstedt, 1945), many surgeons have sought a combination of vagotomy with some other procedure which will overcome the resulting gastric stasis. The first and obvious combination was with a posterior gastro-jejunostomy and the second with pyloroplasty. Excellent short-term results were obtained by Beattie when he was at Leicester in vagotomy combined with pyloroplasty. I began in 1947 to treat duodenal ulcer by vagotomy and gastro-jejunostomy (Holt and Robinson, 1955). I shall summarize the results for the purpose of this discussion. Table I shows that

TABLE I.—RESULTS OF VAGOTOMY AND POSTERIOR GASTRO-JEJUNOSTOMY

Total	Mortality	Stomal ulcers	Hæmorrhages
322	2	2	2

it is a reliable, safe procedure and that it has not been followed by many serious complications. The mortality is below 1% and there have been, so far, only 2 cases of stomal ulceration, 1 of which was proved at operation and the second is very doubtful. There have been 2 cases of hæmorrhage, 1 of which was undoubtedly alcoholic gastritis. The effect of vagotomy on gastric acidity as shown by insulin F.G.A. is illustrated in Figs. 1 and 2. A large proportion

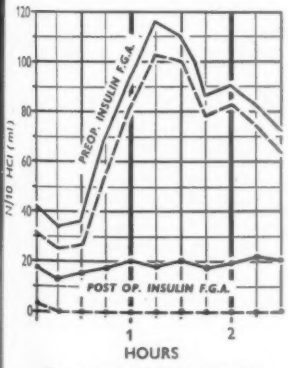

FIG. 1.—Comparison of insulin fractional gastric analysis (F.G.A.) results before and after vagotomy and gastro-enterostomy.

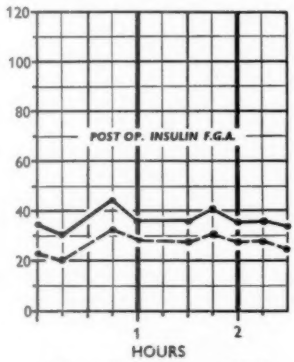

FIG. 2.—Insulin F.G.A. Complete vagotomy with between 20 and 40 units of free acid in the resting contents.

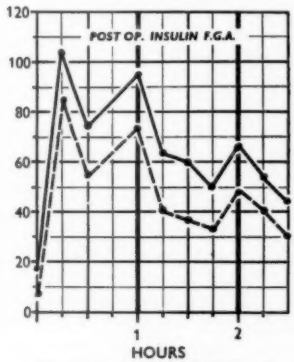

FIG. 3.—Insulin F.G.A. in a case of incomplete vagotomy, with no doubt as to the incompleteness.

of the patients are achlorhydric during this test, but this does not mean that they are completely achlorhydric—they still secrete acid when stimulated by food or histamine but the continuous secretion so typical of duodenal ulcer has been abolished. A smaller group are rendered hypochlorhydric but they too have lost the continuous secretion of nervous origin. Some critics have suggested that the gastro-jejunostomy is responsible for the fall in acidity but this is incorrect. A glance at Fig. 3 shows the sort of response obtained in the presence of posterior gastro-jejunostomy when the vagus has not been completely divided. In our first 200 cases we estimated according to an arbitrary method that vagotomy was incomplete in 12%. Personally I believe our figures are better than this because quite a large proportion

of the so-called failures showed a response of only a few points higher than the arbitrary level allowed.

The results have been assessed by Visick's method (Visick, 1948) and are shown in Table II.

TABLE II.—THREE-YEAR RESULTS OF VAGOTOMY AND POSTERIOR GASTRO-JEJUNOSTOMY USING VISICK'S CLASSIFICATION

	Total		Women	Men under 30
I	99		12	8
II	26	(91%)	3	2
III S	7		—	1
III U	12		4	2
IV	1	(9%)	—	—
	145			

They have been deliberately weighted towards the unsatisfactory side and the cases have been followed up carefully for at least three years. 9 out of 10 have obtained satisfactory results. Of those available for work, 95% are working and 90% of these are working full time. 75% can eat anything and about 20% find that they are more comfortable if they restrict their fat intake. Our interest is centred in the causes of our unsatisfactory results. The rarity of stomal ulceration and hæmorrhage has already been mentioned and there has only been 1 other patient who has complained of pain which resembled his original ulcer pain. No evidence of recurrent ulceration could be found in this case. On the whole the results in women were less satisfactory, but of the 4 unsatisfactory results 1 was suffering from a definite anxiety state and 2 others were in the menopause. In the third column are the results obtained from patients under 30 who are generally regarded as being particularly liable to recurrent ulceration. There are only 2 unsuccessful cases; the first was put in this class, not because of any complaint of his, but because he was not working on account of loss of appetite and energy. The second had been told he had a stomal ulcer at one of the outlying hospitals. We admitted him for investigation and could find no evidence of ulceration. At the time he was undergoing psychiatric treatment.

The minor complications are listed in Table III. Bilious vomiting was the commonest

TABLE III.—MINOR SEQUELÆ OF VAGOTOMY AND POSTERIOR GASTRO-JEJUNOSTOMY

	Bilious vomiting	Dumping	Diarrhœa	Anæmia	Vit. B deficiency
Severe	3	1	0	—	—
Moderate	7	7	3	—	—
Slight	12	11	8	2	2

complaint. It was present in all the women and in 2 of the men was the sole cause of the unsatisfactory results. In half the cases it has been a later development coming on two to three years after operation. It is a complaint difficult to assess since it often clears up at once when the patient is admitted to hospital. Investigation has been unfruitful in every case. 2 of the severe cases have been readmitted for operation and cured by a method to which I shall refer later. The next complaint has been the collection of symptoms known as "dumping". These have consisted of a feeling of fullness after meals accompanied by sweating and faintness. This has only been severe in 1 case and appears to be improving. The list of complaints is completed by diarrhœa, loss of energy and some restriction in diet, but none of these has in itself been particularly troublesome. The patients who are labelled as "unsatisfactory" have usually had several of these complaints. It is interesting to note that out of the 14 patients who were labelled as "unsatisfactory" 7 have an abnormal psychological background. These results are very similar to those published from the Cleveland Clinic (Hoerr *et al.*, 1952) and, in our opinion, compare favourably with any of the published results of gastrectomy.

The nature of these minor complications suggests that they are the side-effects of the gastro-jejunostomy and are not due to the vagotomy.

Along with many other surgeons I have been convinced of the importance, whenever it is possible, of restoring the normal continuity of the gastro-intestinal tract after a gastric operation. To state it simply, the stomach should empty into the duodenum and not into the jejunum. We began by operating on two of the men who were seriously troubled by bilious vomiting. The gastro-jejunostomy was divided and the stomach and jejunum closed. In order to allow the stomach to empty freely the anterior half of the pyloric sphincter was excised. The results were excellent and we have now extended the use of this procedure as a routine for the treatment of duodenal ulcer. The operation we are now trying we have called anterior pylorectomy. The object is to remove the anterior half or two-thirds of the pyloric

sphincter and if the ulcer is situated anteriorly it is also excised in the ellipse of tissue which is removed. The tissues are then sutured so that the suture line is at right angles to the long axis of the gut. It comes together easily and is a much neater procedure than a pyloroplasty. We have used it in more than 50 cases and so far the results are most promising. The vagotomy which is an essential part of the operation removes the factor of excessive gastric secretion, the pylorectomy overcomes the resulting gastric stasis and allows the gastric contents to pass into the correct part of the intestinal tract, that is the duodenum. We have adopted this new procedure, not because we were disappointed with our previous results, but because we are aiming at something approaching perfection.

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Mr. W. M. Capper:

At the present time, the operative procedures which are being used in this country for duodenal ulcer are gastro-enterostomy, partial gastrectomy by the Polya or Billroth I method, or a vagotomy combined with either a gastro-enterostomy or a modified Billroth I resection. It is often difficult to determine which operation is best in any given case, as there are so many variables in the method by which any one operation is done, and also in the criteria by which the results of operation are assessed. The best criterion of all is whether the patient is really satisfied ten years after his operation. The possible operations are:

(1) *Gastro-enterostomy.*—Thousands of these cases have been studied for many years after operation, and we probably have the truth of the matter when we say that if the operation is carried out indiscriminately for duodenal ulcer, and if the cases are followed up long enough, between 30% and 40% will have a recurrent ulcer (Tanner, 1954). Douglas Clark in 1951 (*see* Table I) showed that a recurrent ulcer may appear at any time up to twenty

TABLE I (Clark, 1951).—GASTRO-ENTEROSTOMY
Cumulative Incidence of Relapses

Year of follow-up	No. of cases	Percentage relapses	
		Severe	Total
1	236	8·89	10·59
2	228	14·47	22·80
5	221	19·45	35·29
10	206	23·30	43·19
20	40	25·00	62·50

i.e. a steady increase at least up to 20 years.

years after gastro-enterostomy; certainly no conclusions can be drawn until at least ten years after operation.

Walters *et al.* (1951) say that the mean interval for recurrence is 9·3 years. The early results are definitely good, and it was probably this factor which misled so many early observers, and may be misleading still when the operation is supplemented by vagotomy. Gray and Williams (1949) have compared 500 cases of gastro-enterostomy and Polya gastrectomy over a ten-year follow-up (Table II).

TABLE II (Gray and Williams, 1949; Mayo Clinic).—COMPARISON 500 CASES (TEN-YEAR FOLLOW-UP)

	Polya	Gastro-enterostomy
Complete relief	85%	72%
Partial relief	15%	5%
No relief	—	1%
Worse	—	22%

The significant feature in this series is that 22% said they were actually worse following gastro-enterostomy. A patient with a stomal ulcer has not only a boring pain which is present almost without interruption during the day, but also runs the risk of a gastro-jejuno-colic fistula, in addition to that of perforation and hæmorrhage. To get things in the correct proportion, however, it must be remembered that the other 70% at ten years have complete relief and are on the whole better than the gastrectomized patients.

(2) *Billroth I gastrectomy.*—This operation, which is such a very good one for gastric ulcer, shows a high recurrence rate when used for duodenal ulcer (Table III).

TABLE III

		Billroth I		Polya	
	Amount resected	No. of cases	Proved recurrence rate	No. of cases	Proved recurrence rate
Capper and Welbourn (1955)	<70%	353	8%	706	2%
	>70%	226	1%	783	1%
Goligher (1955)	75%	80	14%	106	1%
Wallensten (1954)	67%	170	8%	276	<1%
Rodgers and Welbourn (1955)	67–75%	27	7%	75	0%
Ordahl *et al.* (1955)	75%	35	28·6%	64	6%

In 1951, I analysed 37 of my own cases and found a recurrence rate of 13%, since when I have not used the operation for duodenal ulcer. Undoubtedly this figure could be lessened if 85% of the stomach was removed, but the lowered recurrence rate is then more than counterbalanced by the side-effects of diminished reservoir capacity of the gastric remnant. I personally do not think that more than 70% of the stomach should be removed for duodenal ulcer, except in special circumstances, because it may be followed by serious loss of weight. An interesting feature that comes out of this analysis (Table IV) is that a 70% resection with a gastro-duodenal anastomosis may be a good operation for duodenal ulcer in women. Further work will be necessary before we can be certain on this point. I personally am not satisfied with the seven-year results of the Polya operation in women, and have used either a Billroth I or von Haberer anastomosis in this sex for the last four years.

TABLE IV.—PROVED RECURRENCES AFTER BILLROTH I FOR DUODENAL ULCER

Sex Variation

		Billroth I	Polya
Wallensten (1954)	Men	10·8%	1·1%
	Women	1·7%	0%
Rodgers and Welbourn (1955)	Men	12·5%	0%
	Women	0%	0%

(3) *Polya gastrectomy.*—This operation has also been carried out for many years. The ten-year results are known and many series of cases have been fully investigated at a sufficient interval to be able to say that we have probably arrived at the truth of the matter. The incidence of recurrent ulceration is low. Capper and Welbourn (1955) estimated it as 2·4% for proved and suspected recurrent ulcers in 1,489 cases. There are, however, side-effects which we all know about, and for convenience call "the dumping syndrome". Capper and Welbourn found 8% occurrence of moderate and severe dumping symptoms in 1,039 cases. Of course, patients vary considerably in their reaction to this phenomenon. In some cases it is incapacitating, while others do not seem unduly disturbed about it. In addition, of course, vomiting of bile may occur in large or small amounts, and this may be a most annoying symptom. Capper and Welbourn (1955) estimated it as 9·6% severe cases in 1,406 patients.

One further point arises, and that is loss of weight. In a 70% Polya, if the comparison is confined to the pre-operative and post-operative weight, the average patient will actually gain 3 lb. (Wells and Welbourn, 1951). The important thing to remember, however, is that the loss of weight following gastrectomy in general will vary directly with the amount of stomach resected, and that women suffer a greater loss of weight than men when a corresponding amount of stomach is resected (Welbourn, 1953).

Butler (1955) has shown some interesting facts in comparing the fat loss in the stools following a Billroth I and Polya gastrectomy. At three months, the total fat loss on an average diet is roughly the same for both operations, but at one year the situation is different. In the Billroth I cases the fat loss remains the same but in the Polya cases it is two or three times as much as it was. (Of course, some patients *need* to lose weight and in a very small number of cases it may be a satisfactory side-effect of the operation.)

In spite of all these things, however, if the patient is asked his opinion of the operation, 95% say they are entirely satisfied (Table V), and, indeed, they may provide some of the most

TABLE V.—PERCENTAGE "SATISFIED"

Polya

Pulvertaft (1952)		94%–95%
Mercer (1954)		95%
Goligher (1955)	Excellent and very good	90%
	Fair	7% } 97%
	Unsatisfactory	3%

satisfied patients in surgery. No doubt the popularity of this operation in this country at the present time is due to the fact that what surgeons appreciate most is a satisfied patient!

(4) *Vagotomy plus gastro-enterostomy.*—Of the various types of drainage operation added to the nerve section, a low transverse gastro-enterostomy is the most popular. The Vagotomy Committee, under Sara Jordan, in 1951—considering 4,076 cases where a vagotomy had been carried out, after an average follow-up period of nearly three years—found a recurrence rate of 27·7%. The other series show a lower rate of recurrence (Table VI) though in all cases it is significantly higher than after a Polya.

TABLE VI.—RECURRENT ULCERATION (PROVED OR CLINICALLY SUSPECTED)

Gastro-enterostomy plus Vagotomy		
Pollard *et al.* (1952)	4·7%	
Hoerr *et al.* (1952)	6·8%	
Walters *et al.* (1951)	11 %	
Henson and Rob (1955)	12 %	(in 29 months)
Bennett-Jones and O'Domhnaill (1955)	11 %	

Walters in a very careful personal follow-up had poor results in 11%, and says that results get worse with the passage of time.

It is probably true to say that in the hands of the ordinary surgeon there is somewhere near a 10% recurrence rate after a five-year interval. It has been shown, however, that with a gastro-enterostomy alone there is a recurrence rate at ten years of about 20%, and moreover recurrent ulceration may be expected at any time up to twenty years. It may well be, therefore, that the final results of gastro-enterostomy plus vagotomy will probably be worse than 10%. In assessing side-effects of the operation other than ulcer pain, and putting them under the term " abdominal distress", Jordan *et al.* (1952) found that symptoms were present in 21·5%, compared with 18·6% following resection, both being estimated two years after operation (Table VII).

TABLE VII (Jordan *et al.*).—ABDOMINAL DISTRESS (OTHER THAN ULCER PAIN)

	Resection	Gastro-enterostomy plus vagotomy	Resection plus vagotomy
At 2 years	18·6%	21·5%	18·6%
	Persistent Dumping Syndrome		
	6·5%	3·3%	3%

MacPhee (1954), in a special investigation of biliary vomiting, found it occurred in 8 out of 31 cases (26%) as compared with 52 out of 311 cases (17%) where a 3/4 Polya had been done. Fat loss after this operation is not usually serious.

Fox and Grimson (1950) examined 9 patients with meteorism, diarrhœa, and weight loss following vagotomy, and found an average of 85% fat absorption.

Turning to the problem of whether the patient is satisfied, some remarkably consistent figures are given by various observers (Table VIII). About 85% said that they are satisfied at from three to five years, and this is probably the true figure. It is remarkable how closely the figures agree. If gastro-enterostomy had been done alone, 70% are satisfied at three to five years.

TABLE VIII.—PATIENTS "SATISFIED" GASTRO-ENTEROSTOMY PLUS VAGOTOMY

Pollard *et al.* (1952) (100 cases)	85·7%
Hoerr *et al.* (1952) (147 cases)	90%
Grimson *et al.* (1952) (101 cases)	80%
Brooks and Moore (1953) (36 cases)	80%
Walters *et al.* (1951) (44 cases)	86%
Hoerr (1955) (154 cases)	81·4%
Pollock (1952) (511 cases)	88%
Bennett-Jones and O'Domhnaill (1955) (95 cases)	88%

Other effects which should be taken into consideration are that ulcer pain may disappear though the ulcer itself is still present (Walters *et al.*, 1951; Brooks and Moore, 1953). Side-effects of vagotomy such as cardiospasm and hypoglycæmic attacks sometimes arise. Diarrhœa may be troublesome and occurred in 3·5% of Hoerr's cases (1955). Post-operative ileus sometimes causes anxiety, and furthermore there is to be considered the effect of vagotomy on the pancreas. There is some evidence that pancreatic secretions diminish following vagotomy, and Butler (1955) has shown that the hormonal and nervous control of the pancreas are to a certain extent synergistic. His experiments suggest that vagal integrity is necessary for efficient pancreatic function: the nerve "tempers" the pancreas in preparation for the hormonal stimulus. I myself have seen a case of serious pancreatic deficiency arising following vagotomy. One wonders whether the hypochlorhydric vago-

tomized stomach may not be a suitable soil for the appearance of carcinoma as the years progress. In one of my cases I have seen a rapidly-spreading carcinoma of the stomach develop following vagotomy. Personally, I reserve vagotomy for a recurrent ulcer which appears following a 70% partial gastrectomy. It should not be done routinely. I also think a vagotomy with a gastro-enterostomy is the best operation in the case where maintenance of weight is essential, as for example in pulmonary tuberculosis.

(5) *Vagotomy with Billroth I.*—This may very well have its advantages. I look forward to an adequate series where a limited Billroth I with a vagotomy has been done, and has been followed up for at least ten years. Certainly the papers so far presented suggest that this method requires an extended trial (Farmer and Smithwick, 1952; Fallis and Barron, 1949; Moloney, 1954; Wells and MacPhee, 1954; Bennett-Jones and O'Domhnaill, 1955; Johnson and Orr, 1954; Coffey and Lazaro, 1955).

Mortality.—The mortality of gastrectomy is probably more than double that of vagotomy (*see* Table IX). It must be remembered, however, that if the patient with a vagotomy and a gastro-enterostomy has a 10% chance of developing recurrent ulceration during the next three to five years, then the initial risk may be worth while. A recurrent ulcer can be much more serious in its effects than a duodenal ulcer.

TABLE IX.—MORTALITY

Vagotomy plus Gastro-enterostomy		
Jordan *et al.* (1952)	857 cases	1·4%
Hoerr (1955)	154 ,,	<0·5%
Johnson and Orr (1954)	30 ,,	0%
Partial Gastrectomy		
Tanner (1954)	531 cases	1·3%
Goligher (1955)	312 ,,	3·8%
Johnson and Orr (1954)	231 ,,	1·3%

In summarizing, I would like to put forward a plea that the final assessment of vagotomy results be delayed until at least ten years have elapsed. Five-year results only show general trends, and so far the results do not appear satisfactory. I feel that all one can say at the present time is:

(1) In all cases of duodenal ulcer in men, a 70% Polya gastrectomy with an antecolic short loop is likely to give maximal relief over the years.

(2) The absolute indication for vagotomy plus gastro-enterostomy is in those cases where post-operative loss of weight may be dangerous. Where a recurrent ulcer forms following a 70% Polya, vagotomy is also indicated providing the stoma is not stenosed.

(3) The results of Polya gastrectomy in women at seven years are unsatisfactory, and it *may* be better to do a 70% resection with a gastro-duodenal anastomosis in this sex.

The long-term reports on a gastro-duodenal anastomosis combined with vagotomy are awaited with interest.

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Professor A. G. R. Lowdon (Department of Surgery, King's College, Newcastle upon Tyne):

In contributing to this discussion I propose to deal with only two of the many facets of the problem. I shall first report the results of a trial of vagotomy combined with limited gastric resection in the treatment of uncomplicated duodenal ulcer, and then make some comments on the Billroth I procedure.

Vagotomy-antrectomy.—This investigation was carried out with the kind permission of Sir James Learmonth in his Unit in Edinburgh. 54 consecutive patients undergoing operation for duodenal ulcer, or anastomotic ulcer after gastro-jejunostomy for duodenal ulcer, were treated by vagotomy and resection of the gastric antrum.

The rationale of this procedure is that the removal of both the neurogenic and gastric hormonic stimuli may reduce acid secretion to safe levels. In addition I hoped that the fact that the patient retained a relatively large gastric remnant with reduced motility might help to preserve the reservoir function of the stomach and lead to some reduction of post-gastrectomy morbidity.

A recent experimental study in Professor Harkins' Unit in Seattle (Sauvage *et al.*, 1953) showed that vagotomy and resection of the gastric antrum in the dog provided a high degree of protection against the development of experimentally produced peptic ulcer, and it was concluded that the clinical trial of "Antrumectomy and Vagotomy" in patients with duodenal ulcer was based on sound principles. I prefer, for euphony as well as brevity, to call the operation "Vagotomy-antrectomy".

The important detail of the operation is the amount of distal stomach resected. Farmer *et al.* (1951) concluded from post-operative gastric secretion tests that, added to vagotomy, removal of about one-third of the stomach was significantly less effective than removal of half of the stomach in reducing acid secretion. In the series I am reporting the resection was never more than about one-third of the stomach. I admit that this was probably less than all of the antral tissue in some cases, but the clinical results suggest that it was a sufficient resection to achieve considerable and lasting reduction of acid secretion. In all cases continuity was re-established by antecolic gastro-jejunal anastomosis.

The series consists of 54 patients, 51 with chronic duodenal ulcer and 3 with gastro-jejunal ulcer. 3 others had previously had gastro-jejunostomies made, but in these there was at the time of operation active duodenal ulceration and no stomal ulcer. There were 49 men and 5 women.

There were two post-operative deaths, one attributable to severe paralytic ileus in the absence of peritonitis, and the other to anuria. Of the 52 remaining patients 1 has been lost to follow-up leaving 51 for study. Of these 2 have died, five and four years after operation, from causes unrelated to their abdominal condition.

Post-operative barium meal studies have been carried out by Dr. D. R. Maitland in Edinburgh; these showed that barium was delayed in the gastric remnant for two or three times as long as is usual after partial gastrectomy with gastro-jejunal anastomosis. 47 patients were readmitted for reassessment including gastric secretion tests with insulin. These tests showed that the vagotomy had been incomplete in 2 patients. One of these developed a stomal ulcer but the other remains well with a low level of acid secretion. Of the others 28 had no free acid in a night secretion test and 17 had low acid levels.

Most of the patients have now been followed for more than five years; the clinical results are assessed as excellent or good in 40, satisfactory but with limitations in 8 and poor in 3. Several of the 40 patients who are entirely satisfied have had temporary or mild complications or side-effects. One had a rupture of the duodenal stump and a fistula which drained for two months; 5 have had to be treated for anæmia; 6 have had occasional slight "dumping" with lassitude and vasomotor disturbance; 2 have had occasional post-prandial nausea and 3 on infrequent occasions bilious vomiting; 4 have had diarrhœa intermittently; one has had a few attacks suggesting hypoglycæmia; and one who was very well for three years then developed pulmonary tuberculosis.

In the 8 patients whose results have been regarded as moderately successful the side-effects have been more troublesome though the patients remain satisfied with the result of the operation. One has been severely anæmic; 3 have frequent "dumping" with vasomotor symptoms; 1 had troublesome diarrhœa with improvement, however, after two years; 3 have bilious vomiting. 2 of these patients I would class as inadequate personalities.

Of the 3 poor results 1, to whom I have referred, had an incomplete vagotomy and developed a stomal ulcer requiring further operation, and 1 continues to complain of pain and vomiting but does not have recurrent ulceration. The third after being well for three years developed a steatorrhœic stool and severe malnutrition.

After this experience my own conclusions about vagotomy-antrectomy with gastro-jejunal anastomosis are as follows:

(1) The operation is effective in reducing acid secretion and the incidence of recurrent ulceration is low if the vagotomy is complete.

(2) If partial resection of the stomach is to be combined with vagotomy then only the antrum need be resected.

(3) The operation involves all the risks of both gastric resection and of vagotomy—both as regards post-operative mortality and post-operative morbidity.

(4) Vagotomy-antrectomy with gastro-jejunal anastomosis is not advisable as a routine method of treatment of duodenal ulcer.

I wish to emphasize that these conclusions apply to the operation when a gastro-jejunal anastomosis is used. The use of a gastro-duodenal anastomosis with vagotomy and limited resection as suggested by Moloney (1954) may materially alter the incidence of post-operative disturbance and may be worth a clinical trial.

Partial gastrectomy with gastro-duodenal anastomosis.—I would like now to consider the Billroth I type of partial gastrectomy (without vagotomy) and to detail the history of the patient who was the third "poor" result of my vagotomy-antrectomy series.

This patient was well for three years after vagotomy-antrectomy but then began to suffer from bilious vomiting. During the next year he began to have steatorrhoeic stools with loss of weight and then nutritional œdema. Four years after operation he was readmitted with severe and progressive malnutrition. He failed to respond to intensive dietetic measures and developed a psychotic state which was regarded as cerebral beri-beri. I then converted his anastomosis from gastro-jejunal to gastro-duodenal type. At the operation there was no sign of anastomotic ulcer and no dilatation of the afferent loop of jejunum, nor of any other part of the intestine. Improvement in his general condition was dramatic and rapid and he has remained well for two and half years since then.

The only explanation which occurs to me is that his steatorrhœa and malnutrition were due to failure of the duodenal digestive secretions to mix with food in the small intestine. In other patients in whom I have converted Polya type of anastomosis to Billroth I because of severe post-gastrectomy syndrome I have seen improvement in nutrition evidenced by gain in weight. There is experimental evidence that absorption of certain food elements is better after gastro-duodenal than after gastro-jejunal anastomosis, and this is no more than we might expect on physiological grounds. It can be said also in favour of the Billroth I type of operation that it is less often followed by severe post-gastrectomy symptoms than is the Polya procedure.

It appears that the resection for gastro-duodenal anastomosis should be about 75% of the stomach. Harkins *et al.* (1954) have made this their aim and have a low incidence of recurrent ulcer in 149 cases of duodenal ulcer treated by the Billroth I operation. I have experience of 122 patients who have had Billroth I operations for duodenal ulcer within the last five years; 35 of these were primary resections for perforation. There were 2 post-operative deaths and 3 cases of stomal ulcer have occurred to date.

The Billroth I operation merits further consideration but if it is to have a fair trial it must be combined with adequate gastric resection. This is possible in most patients only if the stomach is so completely mobilized, by division of all but one or two of the short gastric arteries, that the wide curve of the fundus can be straightened out.

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Dr. W. I. Card:

Studies of Gastric Secretion in Duodenal Ulcer

Examinations of acid gastric secretion in peptic ulcer using various test procedures have been carried out for many years, but have yielded only little information of value. More precise information may be obtained by measuring the total acid output using a maximal histamine stimulus, a procedure whose results are repeatable within the ordinary limits of biological error. The choice of histamine as a stimulus rests on the hypothesis that it is in fact the actual substance released in the stomach which acts on the parietal cells. The rationale for using a maximal histamine stimulus is as follows:

If histamine is infused intravenously at a constant rate for some hours, we ultimately get a plateau response or output of HCl corresponding to the infusing dose. From a series of observations using different doses made on the same subject, it is possible to plot a dose-response curve. All the mathematical implications of this curve need not concern us except to point out that in a subject given increasing doses of histamine, the output climbs to a level which is the limiting output of that particular subject for intravenous histamine. We have elsewhere (Card, 1952; Adam *et al.*, 1954) suggested that this limiting output is some measure of the parietal cell population of the stomach, the "secretory cell mass," and that this is the chief and, indeed, may be the only parameter which distinguishes the secretory response of one stomach from another. If this hypothesis is true there should be a correlation between the acid output and the number of parietal cells present. Histological examination of stomachs which secrete large amounts of HCl show large numbers of parietal cells, while stomachs which secrete little acid show few parietal cells. It is clearly very tedious to carry out histamine infusions but it is possible to get a histamine dose-response curve by giving increasing doses of histamine subcutaneously with an accompanying dose of an anti-histamine to block the side-effects as suggested by Kay (1953). Such a dose-response curve shows that the maximum output under the conditions of the test is reached with a dose of 0·04–0·08 mg./kg., and 0·04 mg./kg. This is the dose which is used as a stimulus. The points of technique to be emphasized are the screening of the tube in position in the stomach, and continuous suction of gastric juice. It is important to measure the output of acid, that is the volume of juice multiplied by the acid concentration. The output of acid may be shown to be reasonably constant from one test to another whereas curves showing concentrations will vary according to the rate of diffusion of histamine from the injection site. This measurement of the output of acid for one hour under a maximal histamine stimulus gives us some kind of index of what the stomach can do under admittedly arbitrary conditions and the figure obtained probably bears some relation to the parietal cell population of the stomach or "secretory cell mass."

This test is done routinely in the Gastro-intestinal Unit, Western General Hospital, Edinburgh, and the results show that the groups of gastric and duodenal ulcers are well separated, though there is naturally some overlap. The test is not, of course, used for diagnostic purposes but as a guide to the nature and extent of an operation. Chronicity of duodenal ulcers and the intractability of their symptoms are associated with a high output of secretion and it would seem difficult to justify any operation on such cases that does not attempt to depress considerably gastric secretion. One method of achieving this is by a removal of a large part of the acid-secreting tissue. What happens when we measure gastric secretion after such a resection?

My colleague Dr. I. N. Marks has been investigating this and has obtained complete gastric juice collections in resected stomachs, employing where necessary a special dumb-bell-shaped balloon to block the stoma. In this way juice can be obtained free from bile and pancreatic juice. His figures show a mean reduction to a quarter of the pre-operative level. This reduction to normal levels is entirely satisfactory and this particular purpose of the operation may be said to have been achieved.

He has also examined the secretion in cases of proved jejunal ulceration after gastrectomy in which the diagnosis was not in doubt. These figures showed that their mean secretion is similar to the mean of untreated duodenal ulcer patients despite an apparently adequate gastrectomy. The highest secretor of them all, 82 mEq. HCl/hour, suffering from repeated hæmorrhages, had had two gastrectomies at another hospital. The discovery of these high acid outputs in jejunal ulceration despite adequate gastrectomy poses an extremely difficult problem. If a subtotal gastrectomy cuts down the secretion by something like three-quarters, this means that the patient with 80 mEq. HCl/hour post-operatively must have had something like 300 mEq. HCl/hour pre-operatively, a figure which is quite inconceivable. One possible hypothesis that we have got to consider quite seriously is that, in certain people after gastrectomy, parietal cell hyperplasia can occur in the remaining portion of the stomach.

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Mr. Ian Orr:

It is eight years since I reported the early results of 100 vagotomies for duodenal ulcer, and I welcome this opportunity to state that I do not consider that vagotomy alone is a suitable operation for this condition. It suffices to say that 34% of the original patients have had to undergo resection. Of the remainder only 22 are perfectly well and completely satisfied with the operation. Gastric retention has been the most serious complication.

Where vagotomy has been combined with an operation providing drainage the unpleasant sequelæ have been largely eliminated, and it is in combination with other gastric operations that vagotomy takes its place in surgery. Its role is not to cure the ulcer, but to lessen the risk of stomal ulceration.

By no means all duodenal ulcer patients display an excess of nervous secreted acid. In 50% the unstimulated night secretion is normal or low, and for such patients the addition of vagotomy to resection is unnecessary and may well do harm. Where it can be shown that nervous secretion is greatly raised (and many duodenal ulcer patients have an unstimulated night secretion of 40–60 units of free acid) the addition of vagotomy will make no difference to the immediate operative result, but will certainly lessen the risk of recurrence.

No one operation will suit every patient, and selective surgery, choosing the operation or combination of operations most suitable to the individual, will pay the highest dividend.

During the past eight years I have carried out 824 operations for uncomplicated duodenal ulcer. My practice has been to remove the ulcer, performing a gastrectomy adequate to lower hormone secretion, but leaving at least 30% of the stomach, and to add vagotomy only if the night secretion is unduly high. It was in fact necessary to vagotomize half the cases.

2% of the resections were carried out in two stages on account of gross œdema and inflammation around the ulcer. In 2% (mainly women and elderly men) a gastro-enterostomy only was performed. The over-all mortality rate was 1·2%.

Stomal ulcer occurred in 2·4% of the series. All the recurrences to date have been in unvagotomized patients and all responded at once to the addition of a transthoracic vagotomy. Dumping occurred in 2·4%, but was slight in all but 5 cases. 10% of the patients lost weight. 4% experienced diarrhœa but in only 1 case was this troublesome. 76% appear to be completely well. 22·4% have minor complaints but are satisfactory. 1·6% have been unsatisfactory. All except 2 of the stomal ulcer cases have fallen into the satisfactory group since the addition of vagotomy.

REFERENCE

ORR, I. M. (1948) *Proc. R. Soc. Med.*, **41**, 639.

Professor C. G. Rob:

I wish to present our results at St. Mary's Hospital with vagotomy and gastro-enterostomy because they are the opposite to those obtained by Mr. Holt. Out of 100 consecutive operations of this type on patients with uncomplicated duodenal ulcer, 12% have a proved recurrence and a further large number have persistent post-operative symptoms other than dyspepsia.

Professor J. C. Goligher:

Like Professor Lowdon I have been moderately addicted to the Billroth I type of gastrectomy operation for duodenal as well as gastric ulcers. Like him I have been remarkably surprised at the frequency with which this form of resection has proved feasible even for adherent posterior wall duodenal ulcers, and as a really high gastrectomy at that. Like him also I have been very pleased with the immediate post-operative course and operative mortality following it. But unlike him I have been profoundly dissatisfied with the ultimate outcome in many of these cases.

We have recently conducted at Leeds a very careful survey of the comparative late results of subtotal gastrectomy by Billroth I and Polya techniques respectively in the treatment of duodenal ulcer. Each case was interviewed not by a single individual but by a small panel. The panel usually conducted its preliminary assessment before consulting the patient's clinical notes so that its decision was often reached in complete ignorance of the type of operation that had been performed. Briefly our findings were these:

Firstly, that the Billroth I resection is followed by a very much higher incidence of recurrent ulceration than is the Polya—the difference on three-year follow-up being of the order of 17% as contrasted with 3%. In this connexion I should like to emphasize to Professor Lowdon that the resections in the two series were of roughly comparable extent and that there was no question of the Billroth I gastrectomies being in any way skimped. Subsequent X-ray studies on the cases of recurrence and some others showed that they had had perfectly adequate resections. To Mr. Capper I would mention that 4 of the recurrences were in female patients, so that there is no reason to suppose that the Billroth I, or Finney-Haberer modification of it, will be any better in women than in men.

Secondly, that as regards the functional condition of the patients—that is to say their liability to post-gastrectomy syndromes, their nutritional state and their capacity for work and enjoyment of life—there was really very little difference in the results of the 2 operations. The only significant point seemed to be the lesser incidence of bilious vomiting after the Billroth I resection than after the Polya operation. In evaluating these findings I would like to stress the blind and, we believe, unbiased nature of this study.

These observations have cured me of my addiction to the Billroth I resection for duodenal ulcer. In my present view it is a thoroughly unsatisfactory primary operation for this condition, though I admit that in certain cases of SEVERE *bile regurgitation after Polya gastrectomy for duodenal ulcer*, it is justifiable to convert to a Billroth I type of anastomosis and to accept the greater predisposition to recurrent ulceration in order to get rid of this troublesome and often disabling symptom.

There is, of course, one other very telling argument of an historical nature against the Billroth I resection for duodenal ulcer. The man who really popularized the Billroth I operation for peptic ulcer—gastric or duodenal—was von Haberer, who performed thousands of these operations and was for many years the leading advocate of this method of resection. It is therefore very significant that in 1947 he admitted that the Billroth I method was not as satisfactory for duodenal ulcer as was the Polya operation, and quietly dropped it. This seems to me a most damning reflection on the operation.

REFERENCE

HABERER, H. VON (1947) *Zbl. Chir.*, **72**, 496.

Mr. G. E. Moloney:

A survey of my patients after operations for duodenal ulcer has convinced me that the functional results are superior with the Billroth I method.

For duodenal ulcers I have done about 110 Billroth I procedures, without vagotomy, intending the resection to be two-thirds of the stomach, with 6 stomal ulcers to date.

It might be thought that with a recurrence rate of 5–6% for duodenal ulceration after the Billroth I technique I might have reverted to a high Polya operation. The opposite is the case, and I am now doing much lower gastric resections, nearer to one-third than one-half, and using the Billroth I anastomosis, but in addition performing vagotomy.

When, in 1951, I began to add vagotomy to the Billroth I operation, it was with the intention of retaining more stomach in an endeavour to overcome the nuisance of the small stomach remnant which reduces the capacity especially for the main meal. The vagotomy was intended to compensate for the extra portion of the stomach retained. In the first 30 or so resections it was a half-gastrectomy, but latterly it has been about one-third, the intention being to remove the ulcer, the pylorus and the pyloric antrum with its powerful mucosa.

This series of patients now numbers more than 100 (about 110). 45 patients have had their operations for more than two years and in the whole series of more than 100 there is so far no patient showing stomal ulceration. As so much stomach remains the anastomosis is always free of any tension, and, in fact, there has been no known anastomotic leakage. The vagotomy has not added any distressing symptoms in the way of gastric retention, or distension, and there is nothing to indicate that the bowels have been disturbed by it. One woman is mentally peculiar and dumps; and one man has endless post-operative complications. The others are a most satisfactory lot of patients.

The 6 patients with anastomotic ulcers after resections for duodenal ulcer have been treated by resection of the ulcer with an adjacent cuff of stomach and duodenum, vagotomy, and Billroth I anastomosis. None died, and all are in good condition.

This series of more than 100 patients who have had low gastric resection, excision of the ulcer, with vagotomy and Billroth I anastomosis represent, to date, my best results after operations for duodenal ulcer. I will now stand by to recant as the stomal ulceration comes to light.

Mr. Norman C. Tanner:

Surgeons have for long tried to find a test which would enable us to select those patients especially prone to stomal ulcer so that only this group should be subjected to the more extensive ulcer operations. At present we have no reliable test. Night secretion tests have many fallacies, for individual patients go through phases of high secretion initiated by mental and other stresses and also the loss through the duodenum is not measured. Furthermore, if the night secretion test ends at 9 a.m., and the patient customarily eats at 8 a.m., the sight and smell of breakfast, or even the sight of the clock pointing to 8 a.m., may bring his vagus into activity and increase his secretion above that of another patient who has happened to sleep through his test.

It is too early to come to any conclusion about the combination of vagotomy and other curative gastric operations. We must first find out the effect of vagotomy alone, and so my own practice has been to carry out vagotomy plus the simplest "drainage" operation—pyloroplasty. This gives a less complicated issue because pyloroplasty alone is not a curative operation and confuses the issue less. Excision of part of the pyloric muscle is, I believe, unnecessary and it has no greater or less destructive effect on the pyloric mechanism than a simple Heineke-Mikulicz pyloroplasty.

The incidence of gastric ulceration after vagotomy is capable of a simple explanation. If I carry out 100 gastrectomies for duodenal ulcer, I shall find on opening the specimen that 2–4 of the specimens contain an unpalpated gastric ulcer. We may, therefore, be reasonably sure that of every 100 vagotomies carried out some 2–4 of the patients will also have an unsuspected ulcer. It is probably these ulcers, uninfluenced by the vagotomy, which are diagnosed in the vagotomy follow-up.

One point which I have found helpful in cases of prolonged small bowel ileus after vagotomy is that when gastric suction and fluid replacement have been continued for a few days and the patient appears to be making no progress, *intravenous* Pituitrin may help. The patient should have a small stomach tube in situ and suction started; he should be seated on a bed-pan. Pituitrin is then given intravenously at the rate of 0·1 ml. per 15 sec. to a maximum of 1 ml. A watch is kept on the pulse and general condition and as soon as good evidence of flatus being expelled is obtained the injection can be slowed or discontinued. It often has a dramatic and sometimes life-saving effect, provided that the condition is one of ileus and not of obstruction.

Professor A. G. R. Lowdon, in reply**:** With reference to Professor Goligher's remarks about the Billroth I operation, I would like to emphasize that it is not enough to make the resection for gastro-duodenal anastomosis comparable in extent to the resection commonly employed for partial gastrectomy with gastro-jejunal anastomosis. We know that the gastro-jejunostomy has some virtue of its own in preventing recurrence of ulcer: in the absence of this the resection for Billroth I gastrectomy must be more radical. I am not yet convinced that, if this requirement is met, the incidence of recurrent ulcer outweighs the other advantages to be gained by gastro-duodenal anastomosis. Nor am I very impressed by the argument that von Haberer gave up the Billroth I operation for peptic ulcer; all the evidence that I know suggests that he habitually performed what we would now regard as a quite inadequate resection.

I am not prepared to make a confident assertion that the Billroth I operation is better than the Polya, but I continue to plead that it should not be misjudged on the basis of inadequate resections.

Section of Psychiatry

President—W. D. NICOL, M.B., F.R.C.P.

[*February* 14, 1956]

DISCUSSION: AN EXPERIMENTAL APPROACH TO THE PROBLEM OF SIMULATION IN MENTAL DISORDER

Prof. E. W. Anderson (University Department of Psychiatry, Royal Infirmary, Manchester):

I. INTRODUCTION

It is generally agreed that the willed, purposive feigning of a mental illness is both uncommon and extremely difficult to sustain. Nevertheless the possibility of simulation as a diagnosis must be remembered especially under certain conditions, e.g. in imprisonment, civilian and military, and when compensation issues arise. If we adopt the criteria of simulation laid down by Farrell and Kaufman (1943) viz. (1) "that no obvious or frank disease or personality disorder is present, (2) that the individual is consciously aware of what he is doing and the motive responsible for his attitude, and (3) that he is fixed in carrying out a purpose to a preconceived result", the diagnosis of simulation will be made only rarely. Simulants often show an abnormal suggestibility and include many hysterics and criminals, notably thieves (Jung, 1902–3), pseudologists (Utitz, 1918), psychopaths with "a particular tinge of deceitfulness and lack of social conscience" (Braun, 1928) and Sträussler (1919) says of simulants in general "one gets the impression that these people only need to open the sluice-gates which have up till then held back their slumbering pathological 'anlagen' for these to be activated and poured forth in the form of psychotic symptoms".

The incidence of simulation is difficult to assess. Jung (1902–3) found 11 simulants in 8,430 admissions to Burghölzli (0·13%), whilst Brussel and Hitch (1943) found 2–7% of all patients referred to the neuropsychiatric service of military hospitals in the U.S. during the Second World War were diagnosed as malingerers. In general, because of the growth of knowledge of clinical psychiatry, simulation has been on the whole *diagnosed* less with the passage of time. C. Norman (1892) remarked the concern of the authorities at the large number of simulations of mental illness in the British Army of that time. This can be contrasted with the relatively small number of such in the First World War (Good, 1942; Roussy and Lhermitte, 1918) despite the ostensibly greater encouragement and opportunity in war. Simulation may be divided into three broad groups:

(1) Clinical simulation; (2) ritual simulation; (3) experimental simulation.

In the first, mental disorder is usually feigned to escape from an intolerable external situation. It may take the form of voluntary and intentional exaggeration or prolongation of a real disorder or of isolated symptoms (Roussy and Lhermitte, 1918). Klieneberger (1921) reported instances of successful simulation of psychoses amongst German prisoners of war (of whom he was one) in an English internment camp in the First World War. He differentiated 3 forms (1) where the mental "symptoms" were supported by artificially induced physical symptoms such as sleepless or vasomotor disturbances brought about by drugs, e.g. caffeine and aspirin; (2) the production of a bogus but well-informed medical history; and lastly (3) (*a*) in a group of psychopaths and psychotics, (*b*) in the healthy. One subject who staged a sham suicidal attempt by hanging and was cut down just in time had a remarkable parallel in the similar attempt of Jones and his associate in a Turkish prisoner of war camp during the same war. The methods used in each case, drugs and careful indoctrination in the phenomena of mental disorder by a doctor in the camp may also be remarked. The role of suggestion by doctors in the production of the so-called prison psychoses so clearly related to simulation probably explains the evidently extreme rarity of these in this country supporting the view of Bleuler (1937) that the "psychopathic delusional states in degenerates" (Birnbaum) would diminish greatly if less attention were paid to them. Social and racial factors may also play a part as in the cases of hysterical puerilism reported by Sträussler (1911).

(2) *Ritual Simulation*

Under this heading are included a number of cases reported by the anthropologists. Thus after the ritual "death" and "rebirth" of boys in the ceremonies of initiation to the Kakian association in Ceram, the candidates on return to their village must feign ignorance of their former life, pretend they do not recognize their houses, the use of common objects, that they cannot speak, &c. (Frazer, 1913). The same author reports similar behaviour amongst some African tribes. In these cases it is questionable whether this is sheer pretence or whether under the influence of powerful affects a state of abnormal consciousness has been induced, or whether as in the hysterical states a mixture of both, since as most writers affirm, e.g. Vorkastner (1928), Jahrreiss (1928), Sträussler (1919), and in agreement with our own experience, the dividing line between conscious and unconscious simulation is nebulous.

(3) *Experimental Simulation*

Previous experimental studies have been few. Jung (1902–3) believing that the symptom of "vorbeireden" arose in a state of divided attention sought to provoke this experimentally. Using his Word Association method, he distracted the subject's attention by metronome beats and asking the subject to draw a line of a given length at the same time as the stimulus word was given. With increasing rates of metronome beat, Jung noted an appreciable decrease of "inner" associations and a notable increase, *inter alia*, of sound associations and failure to apprehend the stimulus word. Henneberg (1904) asked naïve subjects to feign mental illness and noted the great frequency of "vorbeireden". Hübner (1918) and (1919) trained a number of naïve subjects in the simulation of mental illness. One of these, a woman with mild hysterical symptoms, so successfully imitated a patient with a retarded depression that she deceived an experienced psychiatrist. In 1921 O. Loewenstein and his associates R. Mentz and F. Bausch asked 32 subjects to simulate neurological disorder. All the signs produced were those characteristic of hysteria and did not differ objectively from these. Only a few simulated psychiatric disorder, one a severe depression. Bender (1938) carried out experiments in which normal subjects were asked to simulate mental defect using the Bender Gestalt test.

"*Vorbeireden*"

This, the symptom of the "approximate answer", "talking past the point" or "paralogy" was first described by Moeli in 1888 as follows: "The answer is wrong, it is true, but it bears nevertheless some relationship to the sense of the question and shows that the sphere of appropriate concepts has been touched." Thus a sixpence is called a "shilling", a postage stamp "paper" and the like. Ganser (1898) described a "specific twilight state" of which "vorbeireden" was the central and essential feature and which Ganser regarded as hysterical. Nissl (1902) contended that the "vorbeireden" was identical with that found in catatonics and arose from their negativism. In the ensuing controversy the overwhelming balance of opinion turned against Nissl and the hysterical nature of the syndrome was regarded as established. Modern opinion, however, is tending to swing back and Mayer-Gross, for example, has seen a number of cases of Ganser syndrome who later developed a chronic schizophrenia without a clear line of demarcation between the two pictures. The difference between Ganser "vorbeireden" and that found in schizophrenia is less formal perhaps than some (e.g. Jung) have believed.

Henneberg (1904) objected to the term "paralogy" since this was already used to denote the similar schizophrenic disorder. There is some confusion over the relationship of Ganser syndrome to pseudodementia. Thus Mayer-Gross *et al.* (1954) regard them as identical. But Stertz (1910) noted an absence of clouding of consciousness in his pseudodements which is always present in the Ganser state, which accords with our experience. Further, whilst the "vorbeireden" is identical in each and invariable in Ganser it is not always present in pseudodementia. It would seem desirable therefore to separate the two. Henneberg points out that "vorbeireden" may occur under many abnormal as well as in certain normal conditions, e.g. sleep drunkenness, playfulness and preoccupation. Unskilful examination may evoke it as Moeli and many others have stressed. Sträussler (1911) believed the symptom due to a "narrowing of the field of consciousness", distractability and retention disturbance with a loss of associative capacity leading to a faulty recognition of objects. Pick (1917) relates the symptom to a perceptual disturbance in which wholes are not apprehended due to a narrowing of consciousness; he indicates the part played by disturbances in the distribution of attention.

Hahn (1920) pointed out that Pick's view did not explain disturbances in more complicated performances, e.g. arithmetic, and did not explain how the part apprehension arose. Hahn basing his conclusions on the development of colour perception in the child believed that incorrect naming of colours by adults did not arise by chance. In a series of Ganser patients he sought to show that their incorrect naming of colours was a regression in colour perception to an earlier developmental level conditioned by the disturbance of consciousness. The Ganser patient cannot grasp wholes any more than the child or the imbecile can, but whereas in these the inability is due to a defect of previous experience, in the adult Ganser patient it must derive from faulty reproduction, in which, however, the will to answer perversely and to apprehend only a part of the whole may be a factor. This seemed to be the case in some of our simulants. Liebermann (1954) propounds a dynamic interpretation and sees in "vorbeireden" a compromise between the patient's flight from reality and his desire to keep contact with it. Weiner and Braimann (1955) regard "vorbeireden" and loss of personal identity as an attempt by the patient to deceive himself and others by rejecting personality and cognitive functions. Anderson and Mallinson (1941) reported some cases of Ganser syndrome and considered that "vorbeireden" bore a strong resemblance to schizophrenic thought disorder and that formally it was difficult and at times impossible to separate them. We indicated the need for further study of this symptom which formed the starting point of this investiga-

tion. Recent contributions to the problem of simulation of mental illness have included diagnostic studies by Ossipov (1944), Moersch (1944), Davidson (1950), case reports by Good (1942), Atkin (1951) and Wachspress *et al.* (1953) who found projective tests of diagnostic value, psychoanalytic studies by Menninger (1935) and Eissler (1951), but no essentially fresh viewpoint has emerged from these.

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Dr. W. H. Trethowan (Senior Lecturer in Psychiatry, University Department of Psychiatry, Royal Infirmary, Manchester):

II. EXPERIMENTAL DATA

This experiment was designed to investigate certain aspects of the clinical pictures of simulation presented by normal subjects. The focal point of the investigation is on the psychological factors which underlie "vorbeireden" and other forms of approximate answer, and some of the findings are compared with analogous observations made during the examination in a number of patients with both true and pseudodementia.

Method.—18 undergraduate psychology students (13 men, 5 women) were asked to simulate mental disorder. None was forewarned and each after testing was asked to say nothing of the procedure. No subject had any substantial psychiatric knowledge which might have modified the results. Specific inquiry was made into this point.

The Procedure: The subject was briefed by leaving him alone for 15–20 minutes with a sheet of instructions stating the general purpose of the experiment. The subjects were asked to feign mental abnormality for some reason best known to themselves and were informed that they would be then examined by a psychiatrist as if they were genuine patients. They were told they might behave in any appropriate way.

The subject was then interviewed, the procedure being standardized so far as possible and all interviews carried out by the same investigator (E. W. A.) who tried to maintain a similar attitude on each occasion. Two other investigators acted as observers of the subject's behaviour and a secretary recorded all answers to questions verbatim. The interview proceeded to a set plan, similar in every case, and consisted of a series of questions in pre-arranged order. To elucidate further some of the answers supplementary questions were interpolated from time to time at the examiner's discretion. This system allowed for flexibility and ensured the same ground was always covered.

In the first part of the interview the subject's (supposed) complaints were investigated and he was questioned on anomalies of mood, delusions, passivity feelings, perceptual disturbances, &c. In the second part orientation, memory, concentration, general knowledge and his performance in simple mental arithmetic were tested.

After an hour's interview the subject was told he should stop simulating. A retrospective inquiry followed (also recorded verbatim) during which the subject was interrogated on the replies given during the examination. Information was sought on the subject's sources of pathological material and why certain kinds of deliberate error had been made and what he had had in mind at the time.

Comparative Investigations

These were made on three other groups of subjects:

(1) *A normal group* of 50 volunteers drawn from the hospital administrative and technical staff together with some nurses, medical, and P.S.W. students. All were asked to co-operate normally.

(2) *An organic group* of 25 patients with dementia ranging from mild to severe, and unequivocal evidence of cerebral disease.

(3) *A pseudo-dementia group* of 10 patients. Only one of these showed a classical Ganser state. The diagnosis of pseudo-dementia was made after several observations.

Although the method of examination of these three groups was similar to that of the experimental subjects since identical questions were given in the same order, the conditions of examination differed in individual cases. The briefing and the retrospective inquiry were omitted; nor was the whole examination carried out in all groups. In the normal and the organic groups only the testing of the sensorium was carried out. Thus the comparison of these three groups with the experimental group relates only to this aspect of the examination. To facilitate this comparison a system was devised, essentially similar to that devised by Whitley (1911) for scoring the responses of patients asked to repeat a given series of digits, but here the procedure was modified and extended to cover all questions, each answer being allotted a point-score depending on the number of mistakes it was possible to make. This system permitted comparisons between one subject and another and between groups of subjects.

Clinical Pictures of the Simulant Group

With few exceptions none closely resembled well-defined psychiatric disorders or syndromes. Even the better performances lacked consistency and were ill-sustained. These states then merely approximated to the familiar clinical categories (Table I).

TABLE I.—PSYCHIATRIC DISORDERS SIMULATED BY 18 EXPERIMENTAL SUBJECTS

Diagnosis	No. subjects
Simple depression	2
Depression with amnesia	2
Paranoid depression	3
Other paranoid states	5
Simple amnesia	2
Feeble-mindedness	2
Epilepsy	1
Hysterical puerilism	1

For instance *Subject II* was grandiose claiming to have produced a political thesis which, though a masterpiece, had not yet been appreciated as such. In relation to this he complained of persecution by enemies in the disguise of friends plotting to harm him, and of auditory and visual hallucinations. On mental testing he showed definite "vorbeireden" and fatuous or buffoon-like confabulations. For example: Asked to repeat digits he responded with a series of unrelated numbers which he said later, on retrospective inquiry, were the telephone numbers of his friends. It appeared that the easier the question the more difficult did he find the answer. Thus asked to add 5 and 11 he did this correctly; 9 and 8 was, he said: "a year older"; and 2 and 3 was: "a difficult one".

Subject 12 was possibly the most interesting. He gave a false name, as did some of the

others, said he was the author of "Mein Kampf" but at the same time was aged 19 and a University student. After this "double orientation" he expressed some delusional ideas during which he stuttered profusely and became increasingly agitated. At one juncture he rose from his chair, stated that he had seen a face leering at him through the window and insisted that all the windows be shut. Of interest was his continuous talking past and around the point producing a strong impression of disordered association, e.g.

Q. "Do you smoke?"

A. "You see the thing is it's best to use Cherry Blossom. You have to clean your shoes because the shoes are the most vulnerable part—if they have a polished surface the gamma rays can't get at you. You have to walk on the edge of the pavement, if you leave it you have absolutely had it because they have a way of keeping these rays running right along the edge of the pavement."

Q. "Do you have any morbid ideas?"

A. "Well it's the branches on trees—it's the way they stick out—they're pointing in all directions—you just can't take them, they rustle and they speak. You have to be very careful about these trees, they're black and significant, you must be careful and not let them touch you."

Even this picture lacked consistency and later on the subject's answers became more and more normal. He subsequently admitted that increasing fatigue made the role difficult to sustain. A similar observation regarding the pull of the reality situation was made by a number of the other subjects.

Subject 18 simulated a picture different from all the others. She behaved in a childish ridiculous way; was coy, flirtatious, capricious and evasive. She fairly successfully produced an impression of a shallow immature and brittle hysteric. On mental testing her fatuousness increased to buffoonery. Asked to repeat a series of digits she replied: "1-2-3-4-5" on two occasions. To: "Who is the Prime Minister?"—"A man!"; "How many sorts of cards in a pack?"—"Lots of red ones and black ones"; "The difference between ice and glass?"—"It makes a nice noise ice—a tinkling noise when you rattle it"; Retrospectively she said she felt as if the role were taking hold of her. It also seemed as if she experienced a split for she spoke of "two processes of thought, one thinking deeply to prevent me from thinking deeply".

Not all gave approximate answers or "vorbeireden". Some produced a sprinkling, only a few a substantial number of such responses, though there were, all told, sufficient to provide some information as to the mechanism of production. This was not always so straightforward as in one case who asked why he made 26 and 18 equal to 43 replied that he had felt he should give if not the right answer then something very near it. In many cases the matter was more complicated. One subject who made four times thirteen equal to 54 stated that she at first decided to say 39 (3 x 13) then to change it to 49 as being nearer the correct answer but further decided to "mess the answer about a bit" and finally replied: "Fifty-four". Despite this triple displacement the answer was given reasonably promptly. Another subject said of his reasoning: "Supposing I am asked to add 2 and 2. The answer comes: 4. What shall I do? Give an approximate answer: 5. No, that's not good enough—say 6." He later perceived the fallacy and realized that genuine patients did not usually give approximate answers of this kind but only those who knew the real answer and were trying to simulate.

The transposition and reversal of some of a given series of digits was a type of approximation given by most subjects. One said he felt that it would appear "more genuine" to get the actual digits in wrong order rather than fail to remember any or substitute new ones. In not all was the rearrangement, transposition or reversal of digits deliberate. One subject: "didn't definitely memorize them but picked out a few here and there and let them come out as they would." Another described an attempt at double-bluff. He first wished to show there was nothing wrong by answering the questions correctly but felt that by slipping in a wrong answer every now and then as apparently unintentionally as possible that he could put across the idea that a genuine disturbance was present. Reversal of digits was, he believed, just the kind of mistake that would appear unintentional. Some missed out digits or gave them in wrong order by deliberately not listening intently when the series were given. Another stated: "The first time you said the numbers I was so busy thinking about how to react I really didn't hear them. That gave me a clue."

The turning of an accidental mistake to deliberate use appeared on several occasions with different subjects, e.g. the reply: "Twenty-one shillings" when the name of the reigning Sovereign was asked. This subject stated later that at the time he momentarily, though genuinely, confused a sovereign with a guinea and at once saw in this an opportunity to simulate a disordered association. (One of the organic patients produced an almost identical response to this question: "A guinea!") The same simulant produced many approximate answers. Asked to identify a number of coins he called them "ovals" and "discs". Later he

explained his replies were a reaction to a part—the shape the coin was represented by on the retina—rather than to the whole coin itself.

These examples illustrate some of the mechanisms underlying the production of vague and approximate answers as produced by the simulant group. Although variable in extent and in the manner of their production the subjects usually felt that the answers they gave must, if wrong, be not too far wide of the mark to avoid an impression of spuriousness. To judge the truth of this, the comparative investigation was carried out on the other three groups of subjects.

Discussion and Results of Comparative Investigations

The difference between the 4 groups of subjects according to the percentage errors of all kinds made (Table II) shows that the pseudo-dementia group did worst making a greater

TABLE II.—PROPORTION OF CORRECT TO INCORRECT POINTS SCORED

	Normals	Simulants	Organics	Pseudo-dements
% Correct points	92·9	68·9	58·4	55·0
% Negative (omission error points)	2·7 } 7·1	18·1 } 31·1	21·5 } 41·6	26·3 } 45·0
% Positive (commission) error points	4·4 }	13·0 }	20·1 }	18·7 }

number of errors than the group of organic patients. The group of simulants did much better. Nearly half approached the average normal performance, though they showed much greater range and variability largely due to two of their members (Subjects 11, 18) who produced a performance more abnormal than any other members of any group and in this respect were approached by a few only of the more dilapidated organics.

Contrasting the responses of each group to each one of the 32 questions on memory, orientation, &c., in relation to the whole performance, few significant differences emerge. The overall pattern of each group is remarkably similar. Those questions which the normals found most difficult to answer accurately proved especially difficult for the organics and vice versa. The same was however true of both the simulants and the pseudo-dements suggesting an endeavour to simulate abnormality by using or exaggerating genuine difficulties. This similarity of pattern is most evident in the number of errors made in digit repetitions which become progressively more difficult as the series lengthen.

The only significant differences emerged in relation to orientation in time. Here the pseudo-dements made over three times and the simulants nearly twice the percentage of errors made by the organics. In relation to the total overall performance of the groups the number of errors in time orientation by the pseudo-dements as opposed to the organics appears significant (at less than 1 in 20). Detailed examination shows that asked the time of day most of the organics could make a guess correct to within an hour or an hour and a half. Vague answers, e.g. "morning" or "afternoon" occurred more frequently with simulants and pseudo-dements; gross errors, e.g. "midnight" when the sun was actually shining, and "7 p.m." when it was 10 a.m., while occasionally produced by very dilapidated organics (only in one of the present series) were much more frequent in the pseudo-dements.

The only other difference on quantitative analysis was a tendency for some simulants to do rather better than expected in the questions asked near the end of the examination. This was due to fatigue for, towards the end some of the subjects experienced difficulty in sustaining the role.

Considering the more qualitative aspects of the answers given some further differences emerge:

If the errors made be divided into positive or commission errors and negative or errors of omission the proportion varies from group to group (Table II). The smaller proportion of negative or omission errors made by the normals can be construed as a measure of their willingness to co-operate. In the organics the ratio of negative to positive error points is almost equal, while in the simulants and the pseudo-dements the proportion of negative error points is increased, the picture being in this respect opposite to that of the normals. This negative bias and the much greater proportion of frank refusals to answer can be interpreted in terms of the lack of co-operation so obviously a feature of the examination of patients with pseudo-dementia and probably reflects the difficulty of obtaining satisfactory histories.

However, it is the type of positive or commission errors which are of greater interest. Considering simple approximate answers of the "two-and-two-make-five" kind normal subjects make a substantial number of these, probably due to anxiety. However, gross "vorbeireden," e.g. calling coins "discs and ovals" although undoubted approximations, were not given by the normal subjects. The simulants made a significantly higher number of these grosser errors than did either of the other two abnormal groups. There was, however, little difference in the proportion of grosser errors made by the organics and pseudo-dements, a circumstance probably accounted for by the somewhat negative and colourless clinical picture produced by most of the pseudo-dements.

As with simple approximations so with the transposition and reversal of digits. The proportion of these errors made by normals was double that made by the organics and more than three times that made by the simulants and pseudo-dements. Nevertheless, although the percentage proportion of transposition and simple approximate errors made by normal subjects appears large it must be remembered that the total number of all errors made by normals is small. Considering total overall performance the pseudo-dementia group made a significantly greater number of simple approximate errors while the simulants lay, in this respect, between them and the organics, though nearer to the latter. There is thus some basis for the belief of the association of this kind of error with pseudo- rather than with true dementia. This, however, does not appear true of transposition and reversal errors since the organics made a significantly higher number of this kind of mistake than either the simulants or the pseudo-dements. It appears, therefore, that if a patient gives back some of a series of digits in the wrong order, or, when asked to repeat, e.g. the months of the year in reverse he transposes some elements of the answer, this is not necessarily a deliberate approximation. It may be due in the first instance to an attention defect or in the second to inability to shift or perseveration.

In fact perseveration is a feature which appears to distinguish sharply the performance of organic patients from that of simulants or those with pseudo-dementia. In 7 patients of the organic group the responses showed marked perseveration; in the responses of 4 others though less striking it was still obvious. In addition perseverative tendencies were perceptible in the replies of 6 of the remaining 14 organic patients. In contrast, no perseverative quality of a gross kind was apparent in the responses either of the experimental simulants or those of the pseudo-dements. On close scrutiny the replies of one simulant and two of the patients with pseudo-dementia showed a slight perseverative tendency which was only doubtfully evident in the responses of a few of the others.

In conclusion it must be stated that although the performance of the experimental simulant group is similar in many respects to that of the pseudo-dements there are sufficient differences between the two to make one wary of making assumptions about the latter based on the retrospective analysis carried out as part of the experimental procedure. Further investigation is required to determine whether such a comparison is valid. Apart from the familiar difficulty of comparing the malingerer with the hysteric it has to be considered whether any person prepared to go so far as to simulate mental, or for that matter any other kind of disorder, can safely be contrasted with one who does so purely in the spirit of co-operation in an academic experiment.

We wish to express our thanks to Miss Doris Bee, M.A., who gave us invaluable help in recording the experimental data.

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Mr. J. C. Kenna (Lecturer in Clinical Psychology, University Department of Psychiatry, Royal Infirmary, Manchester):

III. PSYCHOLOGICAL ASPECTS

In all societies part of the education of the child includes the delicate balance between frankness, simulation, lying, integrity, hypocrisy, &c. By simulation we control anxiety and preserve the appropriate level for social communication and interaction. Most of us live to varying degrees by this mechanism. Rejection of it may become a psychiatric symptom, the obsessional concern with the truth, the compulsive telling of the truth (David Riesman, 1952). Simulation is one of the bases of drama. Simulation occurs in cross-cultural contact. It often occurs in present-day society where economic situations are personalized on a mass scale (Wright Mills, 1951). These types of simulation may be said to have some positive social value.

In Part I brief mention was made of dynamic formulations of the Ganser syndrome and by implication of simulation also. The individual's language behaviour is a compromise formation, a symptom in the same way that non-organic limping is a compromise between complete immobility and full normal function. Liebermann (1954) considers the Ganser syndrome as "a last ditch effort to preserve the ability of the ego to invest in objective reality".

The time taken by the psychiatric examination reported above made lengthy psychological testing impossible. However, one minor hypothesis was put to the test: the subject feigning mental illness presented with a psychological test, has no stereotype to guide him. A Visual Motor Gestalt Test was chosen, both because of its brevity and because its author, Lauretta Bender (1938) has reported on its use with Ganser patients and in malingering.

The test was given to 13 of the 18 student subjects already mentioned. 9 subjects produced abnormal records.

The performance of Subject 18 was the most deviant. She reported that she deliberately incorporated the test into the role she was playing. Card A was drawn with the diamond half imposed on the circle. Introspecting later she says—"The circle was drawn indecisively." Card 1 is drawn rapidly as a single unbroken straight line. Card 2 is reduced to a single wavy line, "I didn't want it to be accurate or exact". Card 3 becomes a very distorted figure 8,—"Just a squiggly line" she says. Card 4: she reproduces the wave line but swings it round and places a wavy square above it joined with a narrow bar. She writes the word "feather" in large rather childish writing. Card 5 again has a steep wave with a small circle surmounting it. She says, "A hat with a pom pom", and again writes "hat" beside it. Card 6 she began with a wavy line trailing off to a short straight line. The vertical line is crossed by the horizontal exactly at 90 degrees and then switches away to the left in a faint curve. This demonstrates clearly that the Gestalt is correctly perceived and deliberately altered. On Card 7 she refused; but makes a large heavy pencil cross on the face of the card itself, permanently damaging it. Asked whether she had given herself up completely to the role at this point, she said "No, there was the pull of reality".

Card 8 is a mass of childish scribble. Such decline in quality is most improbable in a genuine patient.

When finished drawing she was asked to associate to the cards. To Card 2 she says "No", and then, "dominoes." This suggests that her drawing of a wavy line was a deliberate distortion, since she had correctly perceived the pattern. One could thus rule out any genuine perceptual disturbance.

The psychiatrist concerned with the detection of simulation, especially when time does not permit him to see the patient on a second occasion, or limits him to a short interview without benefit of an externally verified history, may be helped by considering the report from a clinical psychologist who has tested the patient.

In some few of the cases of simulation reported in the literature, psychological tests have been used, e.g. Wachspress, Berenberg and Jacobson (1953) report 3 cases from an American Army General Hospital.

Benton (1945) and Rosenberg and Feldberg (1944) report on the Rorschach among military malingerers. There is a small but relevant literature on the extent to which subjects can consciously distort their test results, e.g. Fosberg (1938).

Carp and Shavzin (1950) gave the test to 20 subjects once asking them to make a good impression, and once to make a bad impression. Only 3 of 20 subjects managed to alter their patterns to an extent significant at the 5% level. Gibby (1951) inquired into the kind of individuals who were able to effect the greatest change in their performance. These seemed to be the relatively mature and rich personalities, neither rigid nor restricted.

Feldman and Graley (1954) using two groups of University students, N = 72, found that students could alter their records but the results had more in common with neurotic than psychotic records. Four judges were able to distinguish the faked from the normal records.

As soon as possible after simulation the subjects were given a "normal" Rorschach. The purpose of this was to consider the relation between the personality structure so revealed, and the simulated role as evaluated by the psychiatrist. Results will be published later.

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SUMMARY

An experimental study of simulation of mental disorder confined as far as possible to responses at the verbal level, was made on 18 normal subjects (13 men and 5 women). Special attention was given to the symptom of "vorbeireden" and the psychopathological mechanisms underlying this. In addition, the results obtained by the use of the Bender Gestalt test are briefly remarked. The relevant literature has been surveyed.

Section of the History of Medicine

President—Sir ZACHARY COPE, M.S., M.D., F.R.C.S.

[*March* 7, 1956]

Humphrey Lhuyd (1527–1568)
A Sixteenth Century Welsh Physician

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THE latter half of the sixteenth century witnessed an intense literary revival in Wales. Partly due to the inflexibility of the traditional Welsh metrical patterns, Continental poetic forms had little influence on this movement, and it was essentially as a rebirth of Welsh prose that its force was felt. Occurring at a time of the rapid anglicization of the Welsh gentry, hitherto patrons of the arts, this literary movement virtually saved the Welsh language from extinction. Welsh grammarians and translators, both Protestant and Catholic, wrote not only for the edification of their own countrymen, but were also interpreters and expositors of Welsh literature and antiquities for other Western scholars. Actuated largely by humanistic impulses a significant number of these Elizabethan Welsh scholars were practising physicians, and one of them, Humphrey Lhuyd of Denbigh, was a prominent and influential figure in that literary renaissance.

His father, Robert Lhuyd, belonged to the younger branch of the Lhuyds of Foxhall, near Denbigh. The family name was originally Rosindale, but by marriage had assumed the name of Lhuyd (or Lloyd) an ancient line descended from a Welsh chief, Einion Efell. Henry of Rosindale (now Rossendale in Lancashire) was one of the lieutenants of Henry de Lacy, Earl of Lincoln, from whom he had received a grant of land for his part in the wars of the Edwardian Conquest of 1282. Henry of Rosindale had settled at Foxhall in the Vale of Clwyd in 1288.

Robert Lhuyd married Joan Pigott, and Humphrey, the only offspring, was born at Denbigh in 1527. It is not known where he received his early education, but he took his degree at Oxford in 1547, graduating M.A. in 1551, being at that time a commoner at Brasenose College. Following this preliminary of an Arts degree Lhuyd studied medicine. Few students at that time went on to complete the lengthy and tedious curriculum of the English M.B., some proceeding M.D. at Continental universities. There is no record of Lhuyd obtaining his degree in medicine at Oxford, but the university then did issue a separate licence to practise medicine (Davidson, 1953). Astrology, based on the already obsolete Ptolemaic system of astronomy, was in vogue and had a considerable influence on medical practice, and Lhuyd's first publication was a treatise on astrology, undated, and with no copy now in existence. It was entitled:

> "An Almanack and Kalender, containing the Day, Hour, and Minute of the change of the Moon for ever, and the Sign that she is in for these Years, with the Natures of the Signs and Planets, with divers other things, as it doth plainly appear in the Preface." (Wood, 1813–20.)

In 1552 he translated Thesaurus Pauperum of Petrus Hispanus into English at the request of the Earl of Stafford. The original, written in 1277, was a popular collection from the works of Hippocrates, Galen and Avicenna, and its author who was physician to Pope Gregory X later occupied the papal chair himself (Garrison, 1921). Lhuyd said of him "although he chanced in a barbarous and rude time he was a man of great knowledge and long practice". To this translation Lhuyd added the views of Jacobus de Partibus on

therapeutics together with an original contribution on "the causes and signs of every disease". The book appeared in four editions, the last posthumously in 1585, and was entitled "The Treasury of Healthe".[1]

The book was not intended "to maintain the filthy lucre and blind boldness" of those not learned in the signs and causes of disease but for . . . "such honest persons as will moderately and sincerely (either in time or necessity when no learned physician is at hand . . .) manifest the things herein contained and go about the practice thereof . . ." He desired the gentle reader "not to despise this simple work because it is not garnished with colours of rhetoric and fine polished terms, but rather to consider that Physic is an art content only to be plainly and distinctively taught and nothing desirous to be adorned and decked with eloquence and gay painted sentences . . ."

His last medical work appeared in 1553 and was a translation of John Vassey's book on uroscopy[2]. The method of uroscopy was still prominent in medical practice in the sixteenth century. An edition of Vassey's tract appeared in 1549 and this may have been the one used by Lhuyd in his translation.

In 1553, according to Chotzen (1937), Lhuyd became private physician in the service of Henry Fitzalan, twelfth Earl of Arundel. The date of his appointment is not absolutely certain, but he did, according to his own testimony, serve the family for fifteen years.

Henry Fitzalan was a typical product of the Renaissance in England. A nobleman of wide interests and culture, and living at the time of the dissolution of the monasteries, he had managed to build an important library, part of which had once belonged to Archbishop Cranmer. Lhuyd was not only Arundel's personal physician but was also general counsellor who helped his patron to collect books and manuscripts. Arundel's son Henry Maltravers became friendly with John, Lord Lumley, who later married Jane, Maltravers' sister. The three, Arundel, Maltravers and Lumley, were zealous antiquarians and soon Lhuyd joined with them in their historical studies. The library of the British Museum contains a book, Postel's "De Etruriæ Regionis . . . " which was a gift of Maltravers to Lhuyd in 1556, an obviously well-studied and annotated volume (Williams, 1952). Lhuyd with Arundel and Lumley joined the Society of Antiquaries, and their association became further strengthened when Lhuyd married Barbara, Lumley's sister and heiress. Lhuyd also helped Lumley to build his very important library, the collection following Lumley's death being bought by James I, eventually to become part of the important Royal collection at the British Museum. Lhuyd used these valuable acquisitions of historical works as the basis for his further publications dealing with the history of Wales. It was to that object that he dedicated the rest of his short life, although he continued to practise medicine and to take some interest in politics. His brother-in-law, Lumley, endowed the Lumleian lectures of the Royal College of Physicians in 1581 in association with Richard Caldwell. Originally intended as surgical dissertations, they were soon given on medicine, the outstanding lecture being in April 1616 when Harvey first expounded his views on the circulation of the blood. It is of interest that Harvey was physician to Thomas Howard, a later Earl of Arundel, in 1636.

In 1563 Lhuyd returned to Wales, to his native Denbigh, where he remained until his death in 1568. There he "practised his faculty, and sometimes that of music for diversion's sake, being then esteemed a well-bred gentleman" (Wood, 1813–20). He lived within the walls of the old town and was very active in his historical and literary pursuits. The reasons for his move to Wales are rather obscure; Arundel's palace of Nonsuch was an important political centre, the Queen was a frequent visitor there and Lhuyd's circle of acquaintances must have been influential and powerful.

Henry Fitzalan, however, was the leader of the diminishing but still influential group of Catholic nobility. He had been an active supporter of Mary but had retained his employments on the accession of Elizabeth. Following her illness in August 1562 the Queen had to rebuke Arundel for plotting her succession. In 1564 he had to be restrained at Nonsuch

[1]The treasury of healthe conteynyng many profitable medycines gathered out of Hypocrates, Galen and Auycen, by one Petrus Hyspanus & translated into Englysh by Humfre Lloyde who hath added therunto the causes and sygnes of euerye dysease, with the Aphorismes of Hypocrates, and Jacobus de Partybus redacted to a certayne order according to the membres of mans body, and a compendiouse table conteynyng the purginge and confortatyue medycynes, wyth the exposica of certayne names and weyghtes in this boke contayned wyth an apostle of Diocles vnto Kyng Antigonus. 8°.
Colophon: Imprynted at London in Flete-streate at the sygne of the Rosegatland by Wyllyam Copelande. (No date.) The preface is superscribed: To the Gentilharted Reader—Humfrey Lloyde.

[2]Here beginnith a litel treatise conteyninge the iugemet of vrynes most necessary for al such as be desirouse to knowe the state of their owne bodys or be wyllinge to help theyr frindes, wrytyn in the latyn tong by John Uasse and englished by Humfre Lloyde at the request of the Ryght Honorable the Lord Stafforde. Imprinted at London by Richarde Tottyl . . . 1553. Cum Priuilegio. 8°.

by a royal order, and his star finally set when he was implicated in the Ridolfi plot of 1571. Lord Lumley, also a prominent Catholic magnate, lived at Nonsuch with his wife from 1557 and was successively implicated in constant religious intrigues and in 1571 he spent some time in the Tower. Edith Milner (1904) in her "Records of the Lumleys" quotes several letters written in the early years of the reign, some in cipher, sent by two consecutive Spanish ambassadors, both intimates of Arundel's circle, which show the existence of a conspiracy with Arundel and Lumley directly concerned with it. It is more than possible that Lhuyd, friend, counsellor, and physician to this household, knew of the existence of such activities and of their possible consequences, and it is likely that it would have influenced him to return to the comparative calm of a distant Denbigh.

The National Museum of Wales.

FIG. 1.—Humphrey Lhuyd at the age of 34. (Mezzotint by J. Faber (1717) after a portrait by Mark Gheerarts, the Elder (1561).) His motto is seen (top left corner): "Hwy pery klod na golyd" (Fame is more lasting than riches.)

In the year of Lhuyd's return Lord Robert Dudley, later Earl of Leicester, was granted the Lordship of Denbigh. A man who pre-eminently stood for personal magnificence and pride of caste and his conduct governed by expedient rather than moral considerations, he had been intimately concerned in the early years of the reign in the struggle between the forces of Reformation and counter-Reformation in England. He came from a strong anti-Catholic family but yet had an early affinity with the Catholics purely as a political arrangement as were his later Puritan affiliations. In 1561 Dudley and Arundel had a violent quarrel, partly because both competed for the personal favours of the Queen, but also as a result of the consolidation of power among the great men of the realm with Leicester, Burghley and Walsingham and others on the one hand, Norfolk and Arundel on the other (Neale, 1949). These noblemen when in the favour of the Queen were the true rulers of the country and to be under their patronage was desired by many of the rising class of gentry.

The number of borough representatives in Elizabethan Parliaments increased progressively during the reign until the total number of borough seats in the later years was 372, of which nearly three hundred were gentry (Neale, 1949). This aspiring social class, rising in power, sought corresponding responsibility and membership of Parliament carried with it prestige and dignity. Humphrey Lhuyd sat for the borough of Denbigh in Parliament from 1563 until his death in 1568. It is unlikely that he would have continued as a member without the active support of Dudley who throughout this time held the Lordship of Denbigh. In

a later election of 1572 the Earl wrote a scarifying letter to the burgesses of Denbigh who had dared to elect a representative that displeased him (Williams, 1856). It is possible that Lhuyd's move to Denbigh and his membership of Parliament was due to the direct influence of Robert Dudley.

Denbigh stands in the centre of the fertile Vale of Clwyd, a part of North Wales that in the fifteenth century had been rich in patrons and poets of the classic bardic tradition and in the sixteenth century was again the most important part of Wales concerned with the new learning. Welsh scholars now taking advantage of university education and facilities for travel renewed interest in Welsh history and philology and gave to the language and literature a new life and beauty. Himself a typical example of the new gentleman scholar, Lhuyd on his return to Denbigh became the acquaintance of a group of men of supreme importance in Welsh literary history. One of them was William Salesbury (? 1520–1584), a graduate of Oxford, born at Llansannan, a village in Denbighshire. He was the author, in 1547, of one of the earliest Welsh printed books and, apart from his various works on rhetoric, grammar, and history, he translated into English Thomas Linacre's latinised De Sphaerâ of Proclus Diadochus (1550). He also wrote between 1566 and 1574 a Welsh herbal now known as "Llysieulyfr Meddyginiaethol a briodolir i William Salesbury." It was first published forty years ago from an unreliable manuscript copy of 1763 (Roberts, 1916). An older manuscript copy of 1597 is now available (N.L.W. 4581) (Mathias, 1952). This work is a compilation from Fuch's "De Historia Stirpium", a latin herbal of 1542, and from William Turner's "New Herball" of 1551. Salesbury is best known as the translator of most of the New Testament into Welsh and all of the Book of Common Prayer. These were published in 1567 and were welcomed by Lhuyd in his Fragmentum of 1568. Salesbury dedicated a book on Welsh proverbs to Humphrey Lhuyd also in 1567 with the words:

> "Tithev master hunfre lloyt yr hwn ddleyt y blaen ar bawp o ran gwbledd a theilyngdot pop ryw gorevddysg a boneddigeiddrwydd anianol lle na ddlei vot y gan yti tra amlder o ddiarebion Kamberaig ti ally eisoes ag a vedry ddethol a dichlin niver or ei byrraf a synwyrolaf or diarebion Italaeg ev genysgaddv bopvl dy wlat er mwyn lliosogav yddynt mwy o ddoethineb doethion y wlat hono."
> (And you, Master Humphrey Lloyd, who can claim precedence over all on account of completeness and worthiness in all manner of true learning and natural gentility, although thou mayest not have a great number of Welsh proverbs, yet thou canst pick and choose a number of the shortest and pithiest of Italian proverbs for the enrichment of your own people, adding unto them more of the wisdom of the sages of that land.)

In a letter written to Mathew Parker, Archbishop of Canterbury in 1565, on matters of scriptural translation Salesbury referred to Lhuyd: "Therfor, if it may please you to vnderstaunde of the most famous Antiquarius of all our countrey as well Demetiæ as Venetiae it is even one Mr. H. Lloyd born at Denbyghe in Northwales, & in seruice to my Lorde of Arundel. Thys gentelman after J. Leland & Jo. Bale, of all that I know in thys Isle, is most vniversally sene in Histories & most singlerly skylled in rare Subtilitees" (Flower, 1941). Dr. Robin Flower commented that "It was probably unnecessary for Salesbury to commend Llwyd[1] to Parker, for Llwyd had been for some years before his retirement to Denbigh physician to the Earl of Arundel who was closely associated with the Archbishop in interest in the materials of English history and in the collection and copying of manuscripts. Llwyd no doubt knew well Joscelin, Parker's secretary . . . "

Another prominent contemporary who referred to Lhuyd was Gruffudd Hiraethog, a notable Welsh poet who died in 1564. In a poem of praise to Lhuyd he extols his learning, his knowledge of Ptolemaic astronomy, mathematics and music, and he ends "Perl mewn Ty Parlment yw hwn."—"He is a pearl in the House of Parliament" (Bowen, 1953).

The name of Lhuyd was also known to wider circles of literati. George Owen the Elizabethan historian of Pembrokeshire was well acquainted with his works. He was described by Camden as a "learned Briton", and Lhuyd himself refers often to his other celebrated contemporary as "my freende M. Leland".

Lhuyd's reputation as a historian is founded on three works dealing with the early history of Wales. The first, *Cronica Walliae á Rege Cadwalader ad Annum 1294* was not published, but following Lhuyd's death it remained with Sir Henry Sidney, Lord President of Wales, who arranged for David Powel to prepare it for the press. The work appeared in 1584 as the "Historie of Cambria" (Jones, 1952), and was the accepted standard for early Welsh history until Sir J. E. Lloyd's History published in 1911.

Lhuyd's work is for the most part a translation into English of a copy of the ancient Welsh Chronicle of the Princes, "Brut y Tywysygyon", and he claimed "I was the first that

[1]Lhuyd, like many other sixteenth century authors, wrote his own name in different ways. The various other spellings are Llyd, Llwyd, Lloyd, and Lloyde.

tooke the province in hand to put these things into the English tonge for that I wolde not have the inhabitants of this Ile ignorant of the Histories and Cronicles of the same" (Llanst. MS.). Three manuscript copies of Lhuyd's work exist. The one in the British Museum (B.M. Cotton Caligula A VI) was partly written in the hand of one of Lhuyd's acquaintances, John Dee,[1] and contains many of his marginal notes. Another in the hand of Robert Glover, Somerset Herald, at present in the Ashmolean Museum, was also at one time at Dee's Library at Mortlake (Williams, 1952). The third manuscript is at the National Library of Wales (Llanst. MS. 177).

These three extant manuscripts of Lhuyd's work do not differ in any significant degree. The history of Wales is traced in chronological order from an account of Cadwaladr in Brittany and ends with the defeat and imprisonment of Madog ap Llewelyn after the battle of Cefn Digoll in the 1294 rebellion. Lhuyd's sources for his history can be surmized from the catalogue of Lumley's library made about 1610. It includes the works of Gildas, Mathew Paris, Cornelius Tacitus, Herodianus, and some British Chronicles, all of which Lhuyd refers to in the Cronica Walliae. The British Chronicles may have included a version of the Chronicle of the Princes not now in existence since Lhuyd's history is not a slavish translation of any of the three known versions of the Brut.

Parts of Lhuyd's history are in the realm of folk-tale. He accepted uncritically some of the fables of Geoffrey of Monmouth, and some traditional incidents are given the appearance of fact. Lhuyd was the first to give form to the story of the discovery of America by Prince Madog ab Owain long before Columbus. This was a tale readily acceptable to historians during the latter half of the sixteenth century, at the period of the challenge and enterprise of Elizabethan England. Lhuyd refers to "Francis Loues" who asserted that Christians lived in America before 1492. (In Lumley's library was a book by Francisco Lopez de Gomara, *De La Historia Generall de Las Indias*.) John Dee made a marginal note of this on the manuscript of Cronica Walliae in his possession, and he communicated the information to Hakluyt who included it in his Voyages (V. 80). David Samwell, an eighteenth century Welsh naval surgeon, later revived this account of Madog's discovery (Jones, 1955).

A prominent Welsh scholar has asserted that Lhuyd has not been awarded his rightful place as one of the greatest of the Welsh humanists of the Renaissance (Lewis, 1947). Lhuyd's historical works and the motives that actuated them have recently been carefully studied. Apart from his natural interest in the history of his own country and his consequent efforts to make it available to a wider audience, his Cronica Walliae is also an attack on the works of Polydore Vergil, William of Newburgh, and others who had neglected or dismissed the evidence from the ancient Welsh sources largely because of the language difficulty. His strictures on these authors were continued in his later works.

Lhuyd's Cronica Walliae has also some historical importance in that it was among the first to propound the existence of an early Celtic church in Wales that was independent of Rome and primitively protestant in nature. This theory extended to the early Irish and Scots churches and was accepted by many historians until recent times but it is now known to be without foundation (Hay, 1927). The early Christian Celtic Church, of course, had Roman affiliations. Lhuyd wrote this in 1559:

> "The noble Clerke Ambrosius Telesinus who writing in the year 540, when the right Christian faith (which Joseph of Arimathia taught at the Ile of Avalon) reigned in this land, before the proud and bloodthirsty moonke Augustine infected it with his Romish doctrine, in a certaine Ode hath these verses:
>
> Gwae'r Offeiriad byd
> Nys Angreifftia gwyd
> Ac na phregetha, etc. . . .
>
> (Woe to the worldly priest for whom vice hath no fears, and who doth not preach . . .).
> The Brytaines the first inhabiters of this realme did abhorre the Romish doctrine taught in that time . . . and that may be to us a mirrour to see our owne follie if we doo degenerate from our forefathers the ancient Brytaines in the sinceritie of true religion as we do in other things . . ."

These words and the general trend of his work suggest that even at this time when he was still physician to Arundel Lhuyd was repudiating the religion of his master and friend.

[1]John Dee, of Welsh ancestry (Dee, originally Du, black) was a notorious Elizabethan astrologer, mathematician and geographer (Jones, 1953). He knew Welsh, took an interest in Welsh history, and had many Welsh acquaintances apart from Lhuyd, such as Morus Kyffin, a noted Protestant, and Sion Dafydd Rhys, a medical graduate of Siena, and a renowned Welsh grammarian. The Queen frequently consulted John Dee about her health and he was, by royal command, in consultation with Dr. Baily the Oxford Regius Professor of Physic during the Queen's illness in 1578 (MacNalty, 1953). The Queen had undoubtedly been impressed by his forecast early in her reign when Dee had at the request of Robert Dudley predicted that January 14, 1559 would be an astrologically favourable date for her coronation.

Lhuyd's next work *De Mona Druidum Insula, antiquitati suae restituta . . . et de Armamentario Romano*, was contained in a letter to Abraham Ortelius of Antwerp in April 1568. Ortelius had apparently asked for the meaning of Môn, the Welsh for Anglesey, and the essay resulted. Again Lhuyd attacked the meagre knowledge of Welsh history amongst historians such as Polydore and Hector Boethius. Against them he arrayed a list of classical authorities both Welsh and English. He was particularly severe on Polydore, accusing him of historical prejudice and ignorance. The De Mona was included in Ortelius's Theatrum Orbis Terrarum in 1570 and as an appendix to Sir John Price's *Historiæ Brytannicæ Defensio*, in 1573.

Lhuyd's last work was written on his death-bed. This *Commentarioli Britannicæ Descriptionis Fragmentum* had been previously promised to Ortelius as an addition to De Mona, but Lhuyd's advancing illness prevented him sending any but incomplete notes on the History of Britain to his friend. The work was published at Cologne in 1572. "Auctore Humfredo Lhuyd, Denbyghiense, Cambro Britano. Huius auctoris diligentiam et iudicium lector admirabitur." The following year an English translation was made by a physician, Thomas Twyne[1] under the title "The Breviary of Britayne".

Lhuyd's Fragmentum has been described as an important document in the period of the growth of Protestantism, and his bias to the new faith is detectable throughout the book. Again Lhuyd is severe on historians ignorant of the "British Tongue, which hath driuen many notable men to soche shiftes, that endeuorynge to winde themselves oute of one they haue fallen into many moe, and these more grosser errours". Rowse (1950) states: "what gives his book its chief value is the Welsh knowledge he is able to draw upon, his Celtic angle upon the past . . . He makes the sound—and welcome—point that derivations of the early names of the island are not to be sought for in Greek or Latin but in the ancient British tongue. It is curious that this was not appreciated by the scholars of the time: dominated as they were by the classics they were apt to derive any obscure name from Latin, if they could, or if not, from Greek." The sin of Polydore Vergil and others was to be "so impious, in such wyse to despise the majestie of Antiquitie" (Twyne, 1573).

The work was dedicated to Ortelius. He was one of the renowned geographers of the period and lived at Antwerp, then recognized as the centre of the most advanced geographic thought. It was through Sir Richard Clough, a Denbigh man who was responsible for the interest of Sir Thomas Gresham at Antwerp, that he became acquainted with Lhuyd and his work. In England John Dee and Hakluyt were names associated with oceanic discovery and overseas voyages, and Humphrey Lhuyd in the great map-making decade in England in the 1560's prepared two maps of prime importance in British cartography (North, 1937). These were intended to illustrate matters of topography and history in his latter two works and knowing he was about to die he sent them with the Fragmentum to Ortelius with a tragic and tender covering letter:

"Dearly beloved Ortelius. That day wherin I was constrayned to depart from London I receyued your Description of ASIA and before I came home to my house I fell into a very perillous Feuer, which hath so torne this poore body of mine, the X continuall dayes that I was brought into despayre of my life . . . Howbeit, neither the dayly shakynge of the continuall Feuer . . . neither the lookyng for present death . . . could put the remembrance of my Ortelius out of my troubled brayne. Wherefore I send vnto you my Wales, not beutifully set forth in all poynctes, yet truly depeinted, so be that certeyn notes be obserued, which I gathered euen when I was ready to die. You shall also receaue the description of England, set forth as well with the auntient names as those which are now vsed, and an other England also drawne forth perfectly enough. Besides certein fragments written with mine owne hand . . . Which, also (if God has spared me life) you should haue receaued in better order, and in all respects perfect. Take therefore this last remembrance of thy Humfrey, and for ever adieu, my deare friend Ortelius.

From Denbigh in Gwynedh, or Northwales, the XXX of August 1568.

Yours both liuyng and diyng:

Humfrey Lhuyd."

He died the next day. He was 40 years of age.

The standard account of Lhuyd's maps of Wales, and of England and Wales has been given by Dr. F. J. North. The *Cambriae Typus* was the first that Lhuyd produced but is undated. Some of the names are given in Latin, Welsh and English and there are some accompanying descriptive passages, and clearly the map was intended to have a historical as well as geographical import. It was first published by Ortelius in his Theatrum in 1573,

[1]Thomas Twyne (1543–1613), an M.A. graduate of Oxford in 1568, did not graduate M.B. until 1593. A physician under the patronage of Lord Buckhurst, he was a friend of John Dee and himself no less eminent as an astrologer. Twyne also completed the translation of Virgil's Aeneid, a work commenced by the Welsh physician Thomas Phaer (Munk, 1878).

and was reprinted nearly fifty times, lastly in Horn's *Accuratissima Orbis Antiqui Delineatio*, in 1741. The map of England and Wales was also printed in the Theatrum of 1573 and continued to be printed unchanged until 1595 to be later replaced by Christopher Saxton's map. North suggests that Leland may have been the original source of Lhuyd's maps as well as those of Mercator. John Dee's name again enters, for it seems that he could well have seen Leland's work when editing the Welsh physician Robert Recorde's "Grounde of Arts" in 1561, and it is known that Dee was acquainted with Ortelius and Mercator, as well as with Lhuyd (North, 1937).

Lhuyd gave the maps, the Fragmentum, and his personal letter to Ortelius, into the care of one Hugh Owen, with a note "Mr. Owen fold up these safe and delyuer theym at on Emanuel House at Somers Kay beneath Bylyngesgate to be sent to Antwerp-Vale" (Chotzen, 1937). Owen was, like Lhuyd, in the household of the Earl of Arundel. A devout and militant Catholic, he was involved in nearly every Catholic plot of his time including the Gunpowder Treason. In 1571 he was banished for his part in the Ridolfi affair. This man must have been a close and trusted friend of Lhuyd, a curious association of two men with apparently quite different religious and political views.

Chotzen believed that Lhuyd had some connexion with Arundel even when he lived at Denbigh, and that he did in fact accompany the Earl as physician during his visit to Padua for treatment of his gout, departing early in 1566, and returning in March 1567. The visit was also deemed advisable for Arundel for reasons of political convenience. Dodd (1953) suggests that Lhuyd was with Hugh Owen at the Diet of Augsburg in 1566. Williams (1939) has shown that Lhuyd knew Gruffydd Robert, a notable grammarian and Catholic expatriate, and Lewis (1947) believes that they may have met in Milan in 1567.

Lhuyd undoubtedly knew Italian for he had translated proverbs from that language into Welsh, and his linguistic knowledge is mentioned in Peniarth MS. 132 where heraldic material prepared for Welsh poets is said to be "from the collection of Humphrey Lhuyd of Denbigh who translated them from the French and other languages" (Bowen, 1955).

He may have visited Italy before 1566, however, for he mentioned in his Fragmentum that he had been kicked by a horse during a visit to Italy, and that he was "grieviously pained with sciatica continually the space of one whole year", but that this disappeared after five days' treatment at the waters of Bath. The description of that incident suggests that it had occurred some years previously. Arundel may have taken Lhuyd with him on one of the two visits he made to the Continent between 1558 and 1560.

Lhuyd must have been an exceedingly astute and careful man to have remained on good terms for so long with Arundel and his Catholic associates, and whether he did accompany Arundel to Italy in 1566 or not, he certainly was keeping an eye on Arundel's library in 1568 according to his own testimony in the De Mona. In spite of these affiliations he had produced historical works with a strong Protestant bias, and whilst he had consorted with Catholic conspirators, he had also welcomed the Welsh translation of the Book of Common Prayer. To have a close acquaintance simultaneously with such pillars of opposite faiths as Hugh Owen and William Salesbury, and to have been a Member for a borough under Leicester whilst still being physician to Arundel were rather unique achievements in the religious and political arenas of Elizabethan England.

Lhuyd died at Denbigh on August 31, 1568, and was buried at the White Church in the town where a plaque stands in his memory. In it he is portrayed in Spanish dress and in a praying posture, a desk with a book before him and a sword at his side. Underneath are engraved "eight barbarous English verses" (Wood, 1813–20; Yorke, 1887).

A long Welsh cywydd marwnad, a distinctive elegiac poem was composed by Lewys ap Edwart, a well-known contemporary Welsh poet. It refers to Lhuyd's learning, his knowledge of astrology, languages and antiquities. He left four children, the eldest, Splendian, inheriting the Lumley estates at Cheam in Surrey.

In the age of John Caius and William Clowes, Lhuyd was a minor medical figure. His medicine was empiric and traditional, although he does seem to have relied mainly on well-established remedies such as oxymel of squill and arsenic, to the exclusion of the exotic and comprehensive nostrums of old authority. Nevertheless, it was through his professional work that he undoubtedly exerted some influence on the great ones of the realm, and with the advantage of those associations to collect material for his several works no whit less important for their posthumous publication. The death of this cultured Welsh physician at the age of 40 was a loss to several fields of learning, but his contributions were a noble promise of the full flowering of Welsh and English Elizabethan literature.

I wish to thank Lord Cohen of Birkenhead for his valuable advice.

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Section of Laryngology

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[*February* 3, 1956]

DISCUSSION ON UNUSUAL ASPECTS OF ŒSOPHAGEAL DISEASE

Mr. N. R. Barrett: *Perforations of the Œsophagus and of the Pharynx*

I propose to discuss certain results of perforation of the gullet, and particularly those which are perhaps more familiar to thoracic surgeons than to the members of this Section.

Advances in the surgery of the œsophagus have demanded a high standard of pre-operative diagnosis and, in consequence, many more endoscopies are done than formerly. These investigations are frequently difficult and, even in the hands of surgeons who perform œsophagoscopy regularly, there is a risk of perforation. This mounting incidence has been stressed by many authorities and notably by Jemerin (1948) and by Seybold *et al.* (1950). Moreover it has been emphasized that there are causes other than œsophagoscopy of perforation, such as impaction of a sharp foreign body, stab wounds of the neck, pathological lesions of the gullet itself and spontaneous rupture of the normal œsophagus due to vomiting. The effects of perforations vary according to the site and are influenced by the mechanism. In general the subject can be divided into two separate parts, namely perforations in the neck, and perforations in the lower thorax. The diagnosis and management of these two varieties is different, and is now clear; and unless a patient has a fatal underlying pathological lesion, perforation of the œsophagus should be curable without undue morbidity.

My own experience, during the last fifteen years, covers 22 cases, the depressing details of which are laid out in Table I. The majority of these patients were not seen by me until the serious nature of their complications demanded a second opinion. The facts which emerge are striking; and, though no conclusions could be drawn from so small a series, they are supported by the accumulated experience of many other surgeons. A particular point which my cases emphasize is that to treat a perforation conservatively may succeed; but it is likely to fail in that the patient, who survives the emergency, can develop a mediastinal abscess or pleural complications and these result in prolonged illness and pathological sequelæ which can be virtually untreatable.

Pharyngeal Perforations

It was formerly taught that perforations above the cricopharyngeal sphincter were relatively common. Recent statistics from various authorities deny this opinion.

Some years ago, with Dillwyn Thomas, I reported the histories of two patients which were similar and dramatic (Barrett and Thomas, 1944). In each a general anæsthetic had been given, the one to do a bronchogram in a child, and the other to remove an acutely inflamed appendix. Anæsthesia had been induced by inserting a curved metal airway into the pharynx and administering oxygen, bubbled through ether or chloroform, into the airway. The operations were uneventful until the anæsthetist noticed that the eyelids and face had become puffy. Within a few moments the whole of the head, the neck and the trunk were grossly distorted by surgical emphysema. The first child died of asphyxia before anything could be done; the second was saved by aspirating the air from the root of the neck and maintaining an airway by intubation. At autopsy on the one child a gross perforation of the pharynx was not found; merely a small laceration of the mucous membrane which could have been caused by the end of the metal airway. It was presumed that the gas, emerging from the airway with unnecessary force, had penetrated under the mucous membrane and spread far and wide from this point. This type of emergency is not likely to occur with modern methods of anæsthesia; if it did the treatment is to stop the flow of anæsthetic gas, pass an intratracheal tube to maintain respiration and, if necessary, to deflate the tissues of the neck by incising the deep fascia on either side above the clavicles. The situation is sudden and critical.

Perforation of the piriform fossa by an endoscope is rare in my experience, though the possibility must be constantly in mind if, through spasm of the cricopharyngeal sphincter (ineffective anæsthesia) or faulty posture of the neck, the instrument is not passed accurately. Much useful and entertaining information about how to pass instruments into the œsophagus can be had from a book entitled "The Memoirs of a Sword Swallower".

TABLE I

No.	Sex	Age	Cause of perforation	Result of perforation	Treatment of perforation	Result as regards the perforation
			PHARYNGEAL PERFORATIONS			
I	F.	9	Airway used to give an anæsthetic for appendicitis	Sudden and gross local and general emphysema	—	Died within a few minutes of asphyxia
II	M.	11	Airway used to give an anæsthetic to do a bronchogram	Alarming and rapid generalized emphysema	Intubation and artificial respiration. Aspiration of air from the neck	Recovered
III	F.	2	Put a number of Kirby grips in her mouth and choked as a result	F.B. penetrated piriform fossa and embolized to the heart via the venous system	The perforation was not recognized at the time.	Uneventful recovery without treatment. F. B. removed from the heart later.
			CERVICAL ŒSOPHAGEAL PERFORATIONS			
IV	M.	59	Œsophagoscopy for "anæmia" Negative findings. Went home. 4 days later pyrexia and pains in the neck. X-rays showed a small perforated diverticulum and osteitis of C.5 and C.6 vertebræ	It was felt that the œsophagoscopy could have perforated the diverticulum and caused a small abscess.	Antibiotics and rest	Slow recovery
V	F.	70	Œsophagoscopy for dysphagia due to hiatus hernia. No difficulty at the time and no perforation suspected	Cervical perforation diagnosed 24 hours later— Developed a large mediastinal abscess	Drained in the neck on the 8th day after perforation. Rent in cervical œsophagus found and sutured not very convincingly	Developed profuse fistula which closed after 4 weeks. 4 *years later* patient has a stricture at the site of the original perforation
VI	F.	55	Œsophagoscopy for dysphagia. No difficulty at the time. No lesion found. Perforation not suspected	Cervical perforation diagnosed 24 hours later. Large mediastinal collection formed	Medical treatment with antibiotics for 10 days. Costotransversectomy followed by prolonged drainage	Developed a fistula which closed after 6 weeks. Fistula reopened and became permanent. All attempts to close fistula failed. Died 16 months later after many surgical operations to remedy fistula

later after many surgical operations to remedy fistula

No.	Sex	Age	Cause of perforation	Result of perforation	Treatment of perforation	Result as regards the perforation
			CERVICAL ŒSOPHAGEAL PERFORATIONS			
VII	F.	67	Œsophagoscopy for hiatus hernia. No difficulty at the time. Perforation not suspected	Cervical perforation diagnosed 4 days later. Large mediastinal collection of pus	Medical treatment for 14 days with antibiotics. Then cervical drainage of large fœtid abscess	Healed well after a fistula had persisted for a month. Died 4 months later of pulmonary embolism
VIII	F.	47	Œsophagoscopy and "forcible dilatation" of a "stricture" at the "thoracic inlet". The obstruction was actually in the postcricoid region	Few hours later signs and symptoms of a cervical perforation. Tension pneumothorax next day	Treated expectantly until moribund on 7th day when intercostal drainage was established and a gastrostomy was done as nothing could be swallowed	Condition slowly improved but 4 months later had a tight malignant stricture in the postcricoid region, fixation of the larynx and a tracheotomy.
IX	F.	60	Œsophagoscopy for hiatus hernia. No difficulty and perforation was not suspected	Remained well for 9 days then developed typical features of a cervical perforation	Medical treatment with antibiotics. No obvious collection of pus but radiographs showed emphysema	Resolved spontaneously without harmful results
X	M.	55	Œsophagoscopy for carcinoma of lower third of gullet. No difficulty in passing instrument. Perforation was not suspected	Cervical perforation diagnosed within a few hours	Immediate surgical repair of perforation. Antibiotics and temporary wound drainage	Uneventful recovery in a few days
XI	M.	30	Gastroscopy for a suspected neoplasm of stomach. Some difficulty in introducing instrument; but a perforation was not suspected	Cervical perforation diagnosed within a few hours. This diagnosis may have been wrong. The early management of this case was done by a surgeon not familiar with œsophageal work	Immediate exploration of neck but no evidence of perforation found. It is possible that the œsophagus may have been injured at this operation	Developed œsophageal fistula followed by a mediastinal abscess. Costo-transversectomy. Empyema which required drainage. Excision of mediastinal abscess attempted: failed. Thoracoplasty—5 years later fistula in chest persists

No.	Sex	Age	Cause of perforation	Result of perforation	Treatment of perforation	Result as regards the perforation
				LOWER THORACIC PERFORATIONS		
XII	F.	68	Œsophagoscopy for achalasia. Perforation recognized at the time	—	Immediate thoracotomy. No contamination of mediastinum. Œsophagus repaired and Heller's operation done	Uneventful recovery. Achalasia relieved
XIII	M.	47	Many previous intubations &c. for achalasia. Œsophagoscopy. Nothing could be passed into the stomach	Developed acute upper abdominal pain and difficult respiration as soon as he recovered consciousness	Thoracotomy within a few hours. Œsophagus perforated above the neck of the achalasia. Repair Heller's operation	Uneventful recovery. Achalasia relieved
XIV	M.	61	Gastroscopy by an expert. No difficulty. Perforation not suspected	Became acutely ill shortly after and developed a tension pyopneumothorax after 1 week	Chest explored. Multiple pockets of pus. Perforation could not be found. Chest drained. Antibiotics	Died shortly afterwards. No autopsy allowed
XV	M.	70	Œsophagoscopy for reinsertion of Souttar's tube to relieve dysphagia due to carcinoma	Developed signs of a severe upper abdominal emergency on the next day	Treated with sedatives	Died after 5 days. Autopsy showed that the carcinoma had perforated into the mediastinum
XVI	F.	70	Œsophagoscopy for carcinoma of œsophagus. Stricture dilated. Perforation was not suspected	Condition good for 2 days then developed signs of an upper abdominal emergency	Treated with sedatives	Died after 4 days. No autopsy allowed
XVII	F.	49	Œsophagoscopy for a very large paraœsophageal hernia. Some difficulty in getting round the hernia into the stomach. Perforation was not suspected	12 hours later developed signs of an upper abdominal emergency with crepitus at the base of the neck	Thoracotomy within 24 hours. Pleura vividly inflamed. Perforation found and sutured. Acid fluid in pleural cavity and in the mediastinum	Uneventful recovery at first but developed a small empyema which required drainage

pected

mediastinum

No.	Sex	Age	Cause of perforation	Result of perforation	Treatment of perforation	Result as regards the perforation
				LOWER THORACIC PERFORATIONS		
XVIII	F.	62	Achalasia treated by Heller's operation. Very debilitated at the time	3 days after thoracotomy developed upper abdominal pain. Not considered to be serious at the time	Sudden symptoms of peritonitis on 10th post-operative day. Laparotomy: Peritonitis. No abdominal perforation found	3 days later the patient died with peritonitis and acute parotitis. P.M. the whole length of the incision made at the Heller's operation was open and the mucosa had opened throughout
				SPONTANEOUS PERFORATIONS OF THE LOWER ŒSOPHAGUS		
XIX	M.	40	Sudden vomiting followed by excruciating pain and collapse	Diagnosed as a typical perforated G.U. Chest not properly examined at the time	Laparotomy. Nothing abnormal found	6 days later I saw the patient and found a fœtid tension pyopneumothorax. Died on 9th day in spite of drainage. This patient could have been saved by accurate early diagnosis
XX	M.	45	Vomiting after a large meal. Followed by acute upper abdominal pain and collapse	Diagnosed as a perforated G.U.	Laparotomy. Nothing abnormal found	Died 24 hours later. Typical spontaneous perforation found at autopsy. No previous œsophageal disease. Pleural cavity contained gas, food and bloody exudate
XXI	M.	60	Profuse vomiting followed by surgical emphysema at the base of the neck. Pain then developed	Thought at first to be a perforated G.U. but surgical emphysema not explained	Treated expectantly then developed a pyopneumothorax which was drained	Died after 24 hours. Typical spontaneous perforation found at autopsy
XXII	F.	46	Whilst convalescent from a pelvic operation, she suddenly vomited violently. Immediate severe abdominal pain and collapse	Spontaneous perforation of œsophagus diagnosed	Thoracotomy within 6 hours. Gastric contents removed from right chest. Perforation repaired	Convalescence interrupted by the development of a lung abscess, but eventually complete recovery. This is the first recorded case of successful repair

An unusual case of another type was a girl, aged 2, who put a number of wire hair grips into her mouth and choked. She soon became unwell with malaise, vomiting and a rigor. On admission to hospital a radiograph of the upper abdomen showed the hair grip to be lying below the diaphragm. Assuming that it was impacted in the duodenum a surgeon did a laparotomy, but found nothing abnormal. Subsequent films proved that the wire had moved into the chest and now lay inside the right ventricle; from whence I removed it successfully. The explanation of these events was that the wire, impacted in the pharynx, had been forcibly ejected through the wall of the piriform fossa into the lumen of the adjacent jugular vein, as the child coughed. It had then fallen, under the influence of gravity, through the right atrium and into the inferior vena cava. During the laparotomy it had been carried up into the right side of the heart as a venous embolus. This case is not unique, and others are recorded in which needles, &c., have passed from the pharynx into the deep tissues of the neck.

Cervical Perforations

These injuries are relatively common and are nearly always below, *and not above*, the cricopharyngeal sphincter; they lie in the mid-line of the gullet posteriorly. The explanation given by Goligher (1948) appeals to me. The lesion is generally linear necrosis of the œsophageal wall caused by the pressure of the barrel of the endoscope against lipped, prominent or fixed cervical vertebræ. This accounts for the fact that it often follows an endoscopy in an old person which has been easy; that no suggestion of perforation is detected as the instrument is withdrawn, and that the onset of symptoms can be delayed for a day or two. The diagnosis in such cases is suggested if the patient, on recovering consciousness, complains of pain on swallowing, salivation and tenderness on palpation of the neck. Emphysema and œdema of the tissues are not the first signs because the gas and saliva which lie in the prevertebral space are confined by the deep cervical fascia. The diagnosis is confirmed by lateral radiographs of the neck which show gas bubbles in this space and displacement of the œsophagus and the trachea forwards. Once perforation has occurred saliva and gas are extravasated upwards to the base of the skull and downwards into the mediastinum. A relatively large amount of infected liquid can be present without superficial signs, except œdema of the posterior pharyngeal wall. It is unusual for a collection of this type to descend into the mediastinum beyond the level of the hilum of the lung and it remains confined to the prevertebral space unless it ruptures into a pleural cavity.

The deciding factor as to whether a perforation of the cervical œsophagus leads to an important leak is its situation in the front or the back of the gullet. Posterior perforations matter; anterior or lateral perforations are not nearly so serious because there is no loose plane of cleavage between the œsophagus and the trachea in which infection can spread unchecked. Upon this point depends the success of Davidson's method of anchoring Souttar's tubes with a string tied to the tube and passed out through the front of the œsophagus to a button on the skin.

Since the introduction of antibiotics there has been a tendency to treat cervical perforations expectantly. It is not denied that a few fortunate souls may recover under such a regime; but the majority stand in danger of their lives. My series of cases is principally interesting because of the fates of those patients whose perforations were treated expectantly at first and who required drainage of the prevertebral space some days later. To drive this lesson home I shall give the histories of three in more detail than is available in the table.

Case VI.—A woman, aged 55, complaining of dysphagia, was œsophagoscoped without difficulty and nothing abnormal was found. On the following day she complained of cervical pain and difficulty in swallowing saliva. The temperature rose to 101° F. Antibiotics and conservative measures were maintained for ten days although the radiographs showed that a mediastinal mass was present and increasing in size. On the sixteenth day the abscess was drained by costotransversectomy and the suction tube, which had been passed into the abscess from the thoracic incision, could be felt in the back of the pharynx, behind the gullet, by the anæsthetist. An œsophageal fistula developed at the point of drainage, but her condition improved and the discharge ceased after six weeks. Four months later the œsophago-cutaneous fistula opened once more; the discharge was acid and excoriated the skin. It subsided, and she remained intermittently well for another fourteen months when she was readmitted, and an attempt was made to close the fistula, which had recurred, by thoracotomy and cervical exposure with suture of the perforation. This operation proved difficult and failed. It was complicated by an empyema, and the patient eventually died. In the end it seemed to us that curative treatment was wellnigh impossible.

Case XI.—A man aged 30 was gastroscoped in 1951 because he was thought to have a gastric ulcer. The same evening he developed pain in the neck and malaise. The surgeon diagnosed a cervical perforation and operated next day; but exposure of the gullet was not adequate and no abnormality was found. Within a few hours he developed a profuse discharge of œsophageal contents through the neck and an abscess formed at the level of the upper thoracic vertebræ in the mediastinum. By this time he was very unwell and eventually, with some reluctance, costotrans-

versectomy was done. The drainage of œsophageal contents was profuse and persisted. During the last four years this man has been under my care and I have attempted, without success, to close the perforation, to excise the chronic mediastinal abscess, and to treat the lesion by thoracoplasty. He is now ambulant, but subject to repeated attacks of mediastinal suppuration.

Case VIII.—A woman now aged 47 had a thyroidectomy for Graves' disease twenty years ago and the neck had been heavily irradiated post-operatively. She remained well until nine months ago when she developed dysphagia. A surgeon did an œsophagoscopy and reported that he had dilated a "stricture" at 12 cm. The operation was repeated two months later and the phase "forcible dilatation" was now used. On the following day a perforation of the gullet was diagnosed and a pleural effusion developed. Antibiotics and expectant treatment were applied. By the seventh day the patient was seen by a thoracic surgeon who found her to be moribund and suffering from a tension pyopneumothorax; he instituted pleural drainage, did a gastrostomy and saved her life. After three months of pleural drainage the lung re-expanded but the patient had, by now, lost her voice and could swallow nothing by mouth. She was fed by gastrostomy. On admission to St. Thomas's Hospital my colleague Mr. G. H. Bateman found a tight postcricoid stenosis with fixation of the vocal cords. A tracheotomy became necessary and this was followed by excision of the larynx and of the postcricoid lesion, which had been proved histologically to be a carcinoma. In this case the perforation had not only seriously endangered the patient's life, but had postponed definitive treatment. This patient has since died of carcinoma.

I believe the following statements to be true:

(1) Perforations of the cervical œsophagus are seldom diagnosed at the moment they occur. There is often a latent period before symptoms develop.

(2) The earliest proof of cervical perforation is from lateral radiographs of the neck.

(3) A study of the literature shows that the exhibition of antibiotics alone has done little to influence the grave prognosis of these cases and should not be relied upon to effect a cure.

(4) Thoracic surgeons who have first-hand experience of the early treatment of cervical perforations agree that the correct procedure is prompt exposure of the œsophagus, repair of the perforation, temporary drainage of the wound, and the exhibition of antibiotics. This will save patients who would otherwise die in the first forty-eight hours and prevent much chronic illness. If the diagnosis of perforation is, in fact, wrong no irreparable damage will have been done.

(5) To await events when the infection seems to be localizing is to risk the development of a mediastinal abscess, which may itself be a precursor of a pyopneumothorax. There are serious complications. It is not denied that some cases, treated expectantly, recover.

(6) Late drainage of a mediastinal abscess may save the patient's life, but it carries a high mortality and morbidity: the longer you wait the greater the ultimate risk of persistent œsophago-cutaneous fistula, of empyema, and of œsophageal stricture. Some patients, so treated, become incurable and remain chronic invalids, suffering not only from œsophageal troubles but also from suppurative thoracic complications.

(7) If the patient has a mediastinal abscess when you first see the case, drainage is urgently required. It is not always necessary to drain a mediastinal abscess, which has originated in the neck, by costotransversectomy; there are advantages in using a cervical incision and nursing the patient post-operatively with the foot of the bed raised.

Lower Third Perforations

Perforations in the vicinity of the œsophageal hiatus can be spontaneous and result from severe vomiting when the gullet is normal; they may be due to impacted foreign bodies, to peptic ulceration, to tuberculosis, malignant disease or to endoscopy. I shall not discuss those cases in which the surgeon, taking a calculated risk at endoscopy, penetrates the œsophagus whilst attempting to intubate an obstructing, but inoperable, carcinoma.

If the lower œsophagus is perforated for any cause the symptoms are generally dramatic, and the result, without active surgical treatment, fatal. In practically every case the structures immediately involved are the mediastinal areolar tissue planes and perhaps one or both pleural cavities: but the pericardium, in front, and the aorta, behind, are immediate relations and pathological perforations can penetrate either of these. There are two theoretical ways in which the mediastinitis can develop.

Let us first assume that the normal œsophagus has been ruptured by vomiting. In these cases the tear is generally longitudinal, about 1 or 2 cm. in length and situated just above the diaphragmatic hiatus. On rare occasions it may be total and transverse. The surrounding tissues are at first normal and the mediastinal pleura may or may not be intact. The damaging fluid which escapes from the gullet is principally regurgitated gastric contents, and it causes a fulminating chemical mediastinitis, of which the principal feature is hæmorrhagic necrosis. This fluid gets into the œsophagus as a result of retrograde gastric peristalsis and is sucked through the perforation by the relatively negative intrathoracic pressure. These facts have been confirmed at early operation. When the collection has not already communicated with one or both pleural cavities it looks like an œdematous, dark brown

mass in the mediastinum. If intrapleural rupture has occurred the liquid, aspirated for diagnostic purposes from the chest, contains hydrochloric acid and sometimes particles of food and at thoracotomy the affected pleural membrane is vividly inflamed. If, after perforation, the patient endeavours to relieve his pain by drinking, some part of the fluid taken may also escape; but in general these patients do not drink again and vomiting ceases after the perforation. For the reasons described above, spontaneous perforation of the œsophagus is a lethal condition which can only be cured by immediate diagnosis and early suture of the rent. This was first achieved in 1946 (Barrett) and has been accomplished many times since.

If the lower œsophagus, which is in fact normal, has been perforated by endoscopy and the patient has no immediate cause to vomit, the symptoms of mediastinitis may be somewhat delayed, because the mucus and saliva are not normally grossly infected, unless the patient has oral sepsis. But if a perforation is made above a pathological obstruction septic inflammation is early and serious. An obstructed œsophagus contains pyogenic organisms, and some patients suffering from achalasia or carcinoma have a persistent pyrexia due to this fact. Infections which are primarily caused by pyogenic organisms are not so fulminating as those due to regurgitated gastric contents; but their treatment is equally urgent.

The physical signs and symptoms of lower œsophageal perforation closely mimic those due to posterior myocardial infarction or an upper abdominal emergency such as a perforated gastric ulcer or acute pancreatitis. For this reason some patients die undiagnosed and untreated and some undergo a useless laparotomy. The features are severe epigastric pain, shock due to circulatory collapse, rigidity of the upper abdominal muscles and abdominal silence. The differentiating points are that there is no free gas in the abdominal cavity; there may be a pleural effusion (which is acid in reaction) or a tension pneumothorax and radiographs may confirm these points or show mediastinal emphysema. In addition some patients are cyanosed, presumably because the excursions of the diaphragm are limited, and respiration is painful. Surgical emphysema may be palpable at the base of the neck. A patient who develops emphysema in the neck and has thoracic or abdominal pain has a perforated œsophagus. Samson (1951) emphasized that the voice has a peculiar nasal twang, which is due to the surgical emphysema.

Everybody who has experience of these cases agrees that prompt thoracotomy, after the appropriate supportive measures have been given, is essential. The contents of the pleural cavity must be evacuated, the mediastinum explored and the perforation sutured. Closed pleural drainage should be provided and antibiotics prescribed. If mediastinal sepsis is not already established it may be justifiable to repair a hiatus hernia or to do Heller's operation at the same time but this point will be a matter of individual judgment.

Summary.—Until recent times œsophageal perforations were almost universally fatal. During the last ten years Samson (1951), Weisel and Raine (1952), Overstreet and Ochsner (1955) and many other surgeons have come to the same conclusions as regards treatment and they have reported a high percentage of uneventful recoveries. These good results have *not* been due to conservative treatment or liberal antibiotic therapy. They depend, quite simply, on the application of two golden rules:

(1) As soon as a perforation is diagnosed or seriously suspected the œsophagus must be explored, the perforation found and sutured, and the patient treated with antibiotics and supportive therapy. If in doubt, the dictum which Wallace applied to abdominal perforations applies just as forcibly to the gullet: "It is safer to look and see, than to wait and see."

(2) There is no place for drainage alone in the *early phase*. To drain the peri-œsophageal tissues simply results in a fistula which is likely to be the precursor of serious late complications.

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Professor P. R. Allison (Nuffield Department of Surgery, Oxford):

The purpose of this discussion is not so much to clarify the lesser-known abnormalities of the œsophagus as to bring them from under the shadow of those with which we are more familiar in everyday practice. In order to avoid a dull cataloguing of rare and obscure diseases, an effort will be made to muster them in groups, although further study may show that such grouping is not wholly justifiable.

The association of peptic inflammation of the œsophagus and sliding diaphragmatic hernia is to-day a commonplace, and an excellent description of the pathology has recently been given by Peters (1955). For good reasons, however, the association has been temporarily overstressed, and it is now time to emphasize the occurrence of peptic digestion without hernia, or the frequent presence of hernia without obvious inflammation of the œsophagus. In the former group there are the peptic ulcers caused by severe vomiting especially in pregnancy and pyloric obstruction. One such patient was a young woman who had suffered from dysphagia at the end of pregnancy following jaundice and vomiting. Œsophagectomy was performed for her and it was notable that the stenosis occurred some distance away from the cardia. A further example was a man aged 56 years who was seen in sanatorium with bilateral apical tuberculosis and severe vomiting and dysphagia. He was found to have a carcinoma obstructing the pylorus and secondary œsophageal peptic digestion and stenosis. Such a case is not only of interest to the pathologist, for the bringing up of a Roux loop with side-to-side anastomosis to the œsophagus above the peptic ulcer to relieve his dysphagia, and side-to-side anastomosis to the stomach to relieve his vomiting, gave the patient the greatest comfort and indeed complete absence of symptoms for many months.

The "lower œsophageal ring" reported by Inglefinger and Kramer (1953) and Schatzki and Gary (1953) should be mentioned. It is described as a smooth symmetrical diaphragm-like narrowing at the lower end of the œsophagus, of constant position and dimensions in each patient, with or without dysphagia, according to the tightness of the ring and the eating habits of the patient. Most of the published radiographs of this condition suggest that it occurs at or just above the cardia in patients with sliding hernia. Its dissociation from the effects of peptic digestion is therefore difficult, but there may be no obvious ulceration seen at œsophagoscopy. Superficial œsophagitis has been present in those cases seen by the author but dysphagia has only been severe enough to demand operative relief in two patients.

Case I.—A man of 55 had had dysphagia for fifteen years, and after a mistaken diagnosis of cardiospasm had occasionally used a Hurst's mercury bougie. Radiographs showed a ring-like narrowing of the œsophagus which on direct inspection looked and felt as though a fine filament had been tied in the submucous layer. A small swab passed into the stomach on a holder was felt to slip over a ridge that was equally palpable whether the swab was being passed through or withdrawn. Some œsophagitis was present. At operation the cardia was found to be 5 cm. above the hiatus. The muscle of the œsophagus was incised down to the mucosa 4 cm. above the cardia. It was not hypertrophied and this seemed to exclude cardiospasm of fifteen years' duration. Immediately at the cardia over a distance of only 7 mm. the circular muscle was thickened to 3 or 4 mm. in cross section. When it was cut it felt slightly fibrous but a section removed for histology was described as hypertrophied smooth muscle only. It was completely severed and only the fascia of the œsophagus lightly sutured. The hernia was reduced and the hiatus closed with satisfactory relief of all symptoms.

Case II.—A similar patient was operated upon in the same manner, except that the mucosa itself was incised, biopsies taken and the mucosa and fascia propria resutured. Here the muscle did show some fibrosis as well as hypertrophy, and the squamous mucosa at the narrowed ring was inflamed

A large number of patients with sliding hernia have no demonstrable œsophagitis. It is possible to guess that the abundance of mucus from the mouth, pharynx and œsophagus is protective in such patients but there may be other inherent qualities in the tissues themselves about which we know little or nothing. Some of them have no symptoms from the hernia and the diagnosis may be made during a radiographic examination for heart disease or gastro-enterologic study. An important group are those who complain of severe retrosternal pain radiating to the arm or jaws, where the distinction from ischæmic heart pain may be both difficult and important. In some others grossly abnormal patterns of œsophageal contraction may be found, and these may be associated with dysphagia as in the following:

Case III.—A man of 53 years complained of recurrent attacks of obstruction behind the sternum for both solids and liquids for four years. When they occurred he would beat his breast in an effort to relieve himself. Radiographic screening showed strong muscular contraction occurring evenly over a whole 8 cm. length of lower œsophagus. Œsophagoscopy showed inflammation of the mucosa of such intensity that the cardia could not be identified, but the passage of the instrument put an end to his attacks for a whole year. A later examination, after return of symptoms, confirmed the presence of hiatal hernia, and this was cured surgically.

Œsophageal spasm is an extremely dangerous condition to diagnose. So often in surgical experience it has been found to have covered for months or years an underlying organic condition such as carcinoma or peptic stricture. Spasm occurs secondarily to organic disease, but when full investigations have been completed, may also be found to be the expression of nervous strain and over-anxiety.

Case IV.—A middle-aged man came up to hospital about once a year after three or four days of being unable to swallow even water. Each time it was thought that a carcinoma had been overlooked, but always the intense spasm was overcome by œsophagoscopy and later by bouginage with complete relief. The psychological background of this patient was altogether too complicated for discussion amongst surgeons.

The elaboration of the disorders of mobility particularly in relation to nervous disorders is to be undertaken by Professor Johnstone, but it should be stressed that a hernia has to start in a small way and may allow reflux and all that that entails before it is demonstrable as the bulge on the radiograph that we recognize anatomically as a hernia. There is a danger here that something which is amenable to surgical care may be misdiagnosed as a functional illness.

The abnormal contractions in cardiospasm have been often demonstrated and discussed, but there is another group related to duodenal or gastric ulceration that has received less attention. Here we are on dangerous ground for such ulcers may themselves have the same psychosomatic basis as the changes seen in the œsophagus. These may or may not be related to what has been called corkscrew œsophagus, and idiopathic muscular hypertrophy of the œsophagus. We have seen many of the former, and œsophagoscoped them, but never has one needed resection; neither have we followed one to the grave, so that we have no experience of the pathological specimens.

Case V.—One patient, however, who had had a perforated duodenal ulcer eleven years previously, without any history of indigestion, had complained since the incident of periodic attacks of pain behind the sternum lasting one or two days, and of slight difficulty in swallowing. On November 24, 1952, three weeks after the vomiting of blood, radiological examination showed a duodenal ulcer, a gastric diverticulum, irregular œsophageal movements of the corkscrew type and a hold-up of barium in the lower part of the œsophagus. Œsophagoscopy on December 22, 1952, showed no abnormality. This last was repeated on February 1, 1954, when no hernia was found, but after the pinchcock had been opened there was a sudden prolapse of the gastric mucosa. On May 7, 1954, the duodenal ulcer had healed, the œsophagus behaved normally and the patient's symptoms had disappeared.

In other patients the corkscrew appearance persists throughout life.

That prolapse of hypertophied gastric mucosa into the œsophagus may occur and interfere with normal mobility is indicated by the following case under the care of Mr. J. S. Davidson of Bradford, to whom I am indebted for permission to present it.

Case VI.—In 1948, a man of 48 years complained of a lump in the epigastrium and the vomiting of copious watery fluid. The radiographs showed a marked hypertrophic gastritis. On June 23, 1953, he went into hospital after three days' complete œsophageal obstruction. Mr. Davidson removed a mass of dry food from the œsophagus and passed the œsophagoscope into the stomach, but vision was obscured by adherent debris. Later, œsophagoscopy showed no abnormality and gastroscopy showed a general hypertrophy of the mucosa throughout the stomach. The symptoms of gastritis persisted but the patient had no further dysphagia.

Idiopathic muscular hypertrophy, a condition recently reviewed by Sloper (1954), has only come our way once to be recognized, but it may be that some of the permanent corkscrew patterns will be found to belong to this group. The association with duodenal ulcer has been mentioned in various reports.

Case VII.—Our patient, a man of 41 years, had a small insurance agency, a wife, ten children and a duodenal ulcer. For seven years, when he was irritated, food had lodged in the epigastrium and piled up behind his sternum. He vomited every morning on rising and had frequent attacks of pain in the left hypochondrium. The radiographs showed a duodenal ulcer and, over the years, a corkscrew appearance of the œsophagus with extreme muscular irritability, until in 1950, after a high vagotomy, it became inert. It was resected and replaced by a segment of small intestine.

Sloper mentions that 7 of the reported cases of this abnormality had idiopathic hypertrophy of the pylorus.

It needs to be determined whether the corkscrew pattern that maintains the same radiographic contours over the years, is indicative of the idiopathic muscular hypertrophy of the œsophagus. That temporary corkscrew appearance may be seen without detectable morbid anatomical change in the œsophagus, seems certain. The relation between the temporary and the permanent pattern, if any, needs further study.

It is not often that a simple gastric ulcer occurs so high on the lesser curvature as to cause œsophageal obstruction, but when it does so it is very difficult to diagnose. Its presence may be uncertain on the most careful radiographic and œsophagoscopic examination, but, even

if clearly demonstrated, its innocence or malignancy may be a matter of guesswork. The surgical treatment presents its own particular problems too, and there appears to be a strong indication for our recent attempts to make a new cardia after excision of the old one.

Another cause of obstruction of the lower œsophagus that was recently stressed by Keats and Magidson (1955), is the dilated thoracic aorta compressing the lower œsophagus against the back of the heart. This has occurred particularly in elderly arteriosclerotic females. The obstruction may be completed by the impaction of food. There is no great danger in a carefully conducted œsophagoscopy in these patients.

Unusual aspects of cardiospasm would furnish material enough in themselves for any discussion and so it is only possible to mention a few of them. Although the lower œsophagus, as it lengthens and dilates, nearly always projects into the right side of the chest, one has been seen that prolapsed into the left side. No explanation for this rarity was ever found. Instead of general dilatation of the œsophagus above the cardia there may be a local "blow-out" either to the left or to the right. In such cases the dimensions of the rest of the œsophagus may remain within almost normal limits. The large dilated œsophagus of cardiospasm may become the seat of malignant disease, and Barrett (1956) has recently seen the development of an enormous pedunculated leiomyoma. Such complications may be suspected in a patient who has been relieved by treatment and who develops dysphagia again.

An important though rare concomitant of cardiospasm is displacement of the cardia. This may prolapse into the abdomen or rise into the chest with a hernia. In these circumstances it is only the cardiospasm that protects the œsophagus from peptic digestion. The displacement of the cardia, either up or down, may be missed at radiography, especially if little barium enters the stomach and if the patient is not tilted head downwards. It should, however, be diagnosed at open operation, when the cardia and hiatus must be repaired, to produce competence. If such patients are treated by œsophagoscopic dilatation, however, the herniation may not be appreciated. The relief of the cardiospasm will then cause incompetence of the cardia, severe reflux œsophagitis, and a return of dysphagia, not this time from cardiospasm but from fibrous stenosis. This seems to be one of the weak points in the non-operative treatment. Two such patients have been observed with severe fibrous stenosis and a chronic bleeding ulcer. The one had to be resected, restoration of continuity being achieved by œsophago-jejunostomy. The other was not fit for so large an operation and had to depend on occasional œsophagoscopic bouginage.

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In this paper the discussion will be confined to neuromuscular disorders of the œsophagus, excluding those caused by paralysis, collagenous diseases and hereditary afflictions of the nervous system. Fig. 1 shows diagrammatically the abnormalities to be reviewed. At one end of the group is cardiospasm; at the other, diffuse spasm of the lower œsophagus. Between them are a number of curious distortions, some symptomless, some with severe symptoms. Many of these distortions seem to be constant, others change rapidly from one formation to another but common to those of clinical importance is one constant feature—namely, thickening of the œsophageal wall. These disorders will be analysed in more detail to determine whether there is sufficient evidence to classify them as separate entities or whether they might be considered to be different manifestations of the same disorder.

Cardiospasm is a classical example of neuromuscular inco-ordination. In the established case there is a narrowing at the lower end which holds up food and fluid with the result that the œsophagus dilates. Before the advanced, atonic stage is reached the walls are seldom smooth but appear crenated or rippled, and in response to deglutition vigorous contractions occur which seem ineffective and unco-ordinated. The constricted segment, *lying in* the hiatal canal, may be narrow and beak-like, but often shows an olivary bulge before contracting to its narrowest diameter. The smooth, regular mucosal folds within the narrowing are at times defined with unusual clarity. Barium passes through in spurts which coincide with expiration. Lastly there is a narrow but clearly defined shadow cast by the œsophageal wall. It runs parallel to the barium column except at the narrowed segment where th mural shadow appears much thicker. It is rare to see a mural shadow in the norma

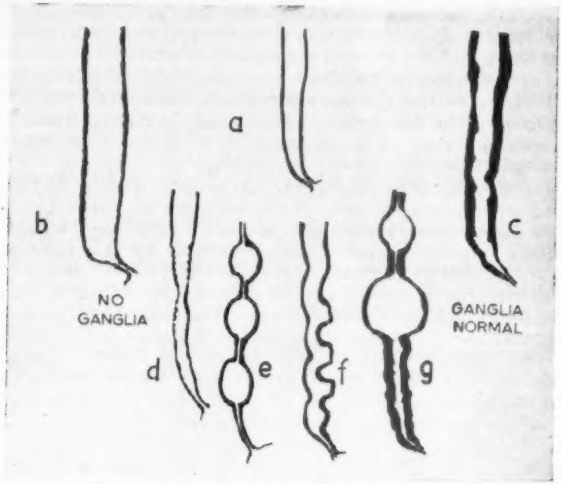
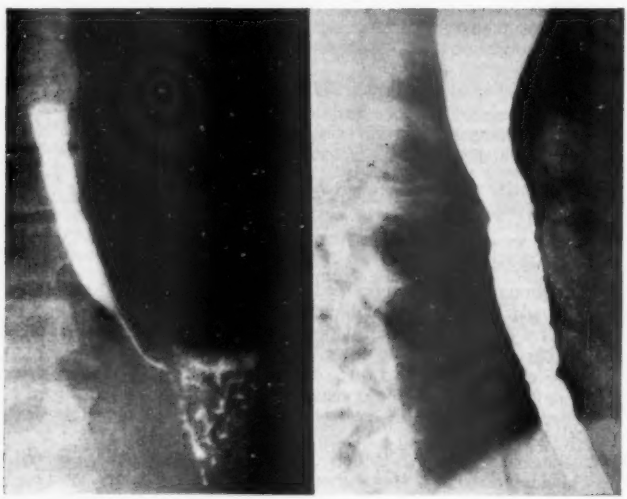


FIG. 1.—Drawing of varieties of radiograms in neuro-muscular disorders of œsophagus. Black line represents wall thickness. (*a*) Very early case, slight spasm at lower end and slight wall thickening. There is no clear indication as to future development. (*b*) Well-established cardiospasm. (*c*) Well-established diffuse spasm. (*d*) Ripple border—senile type. (*e*) Functional diverticula. (*f*) Cork-screw appearance. (*g*) Large diverticula, with diffuse spasm in lower segment. Marked thickening of wall.



A B

FIG. 2.—A, Early features of cardiospasm (*see text*). B, Same patient—upper œsophagus more dilated than lower.

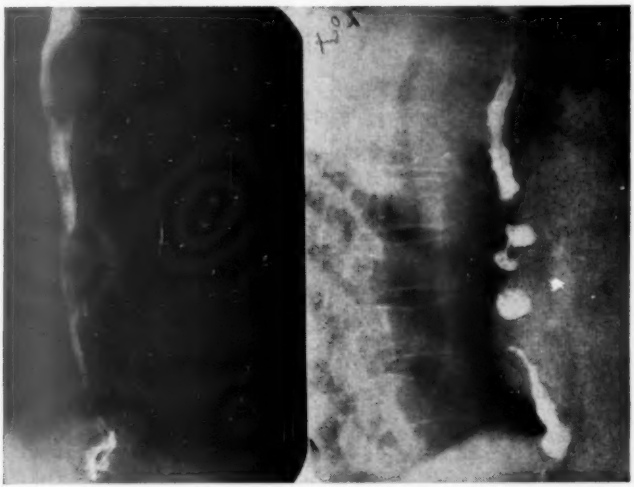
œsophagus, and there is little doubt that its presence indicates thickening, of which the most common cause is muscular hypertrophy (Fig. 2).

The crenated or ripple border is a common finding in cardiospasm but it is by no means pathognomonic, for such a picture is not infrequently found fortuitously in elderly subjects. These undulations have been called "tertiary contractions" following Carlson's classification of œsophageal tonus contractions of circular muscle. Such contractions are not seen by

radiological methods in the normal person and it is unfortunate that the same term should be applied to the abnormal picture. It may be less confusing to use the expression "ripple border" and confine its use to the small crenations illustrated in Fig. 3.

The next stage from the "ripple border" comprises the larger contractions which break up the tubular œsophagus into a string of beads. This picture has also been described as "tertiary contractions", but some have called it "pseudo- or functional diverticula" for these loculi are just evanescent, appearing as the œsophagus contracts (Fig. 4). They may last only a few seconds until the column resumes its normal shape. Œsophageal emptying, however, may be delayed by a series of extraordinary contortions. Rapidly forming constrictions and dilatations appear alternatively in a series of purposeless movements. The activity does not appear to be confined to circular muscle, for the longitudinal fibres may contract vigorously and drag through the hiatus a small pouch of stomach. These contortions are generally limited to the lower segment of œsophagus in which plain muscle predominates. To assess the clinical significance is difficult, for a large proportion of these patients suffer from peptic ulcer of stomach or duodenum, cholecystitis or cancer. Unless there is a clear story of impaction and acute dysphagia (which happened in only one of our cases), the condition should be regarded as one of no clinical significance.

FIG. 3.—Ripple border —senile change—no clinical significance.



A B

FIG. 4.—A, Œsophagus resting phase after passage of bolus—small permanent diverticulum present. B, Active stage of purposeless contractions.

Some patients present a slightly different picture in which the beads are less symmetrical, and may project to one side, a shape which has been called "corkscrew", "knuckle-duster" or "curling". But the beads and curls may rapidly replace one another and it is obvious that they are just variations of the same theme. Serial radiographs taken over several years show that the pouches tend to remain constant in position, and eventually one or more may become permanent, as if they were maintained by adhesions between the adventitia and neighbouring structures. In this group were 14 men and no women. Their ages varied between 44 and 81 years; 10 had symptoms referable to the œsophagus, and of these 3 had active peptic ulcers of stomach or duodenum. One had cancer of the stomach. All 10 showed evidence of wall thickening.

In the next group the ring contractions appear as broad bands of spasm; and at least one of the dilatations has assumed gross dimensions (Fig. 5). In the terminal segment the spasm may cause some irregularity of outline, and the wall may be considerably thickened. Only 3 patients showed this picture; all were men between 48 and 54 years; all complained of dysphagia and substernal pain of varying severity. One had a gastric ulcer, one a duodenal ulcer, and the third was otherwise normal.

Finally there is the disorder of diffuse spasm in which the lower half of the œsophagus fails to distend and appears like a rigid tube with margins often slightly angulated, or

scalloped. Thickening of the wall may be pronounced. In this group we have 4 patients, 3 men and 1 woman whose ages vary from 45 to 55 years. Only one has escaped acute bolus obstruction. All have intermittent dysphagia and substernal discomfort, or at times, severe pain. 2 have active duodenal ulcers.

After considering these varieties of œsophageal contortion, the question arises as to whether they are different entities or variations of the same disorder.

In Fig. 1 cardiospasm was placed at one extremity, diffuse spasm at the other. The reason for this separation lies in the following observations, namely; in cardiospasm the œsophagus is dilated, there is degeneration of Auerbach's plexus and slight muscular hypertrophy; whereas in diffuse spasm there is constriction, the myenteric plexus is normal and the hypertrophy of muscle is marked. Cardiospasm is unassociated with other lesions of the upper alimentary tract whereas diffuse spasm is frequently accompanied by such abnormalities. Finally parasympatheticomimetic agents cause a marked response in cardiospasm whereas in diffuse spasm the degree of contraction and increase in pressure does not differ from the controls.

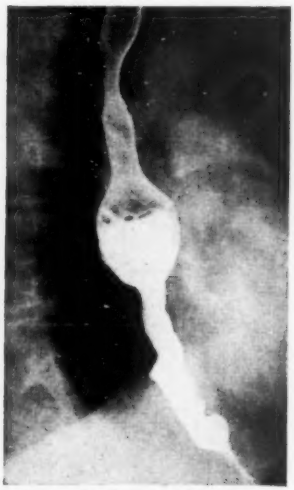
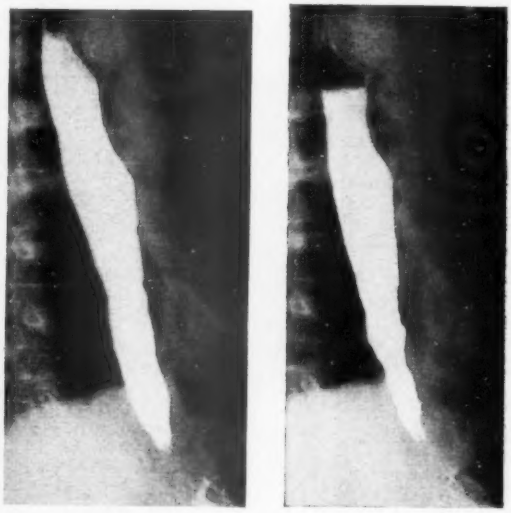


FIG. 5.—Large diverticulum above segment of diffuse spasm. Wall thickening marked.



A B

FIG. 6.—A, Youth 16—signs of early cardiospasm. B, Same patient four years later. Appearances suggest that lesion is proceeding towards diffuse spasm rather than cardiospasm.

If we regard cardiospasm and diffuse spasm as different lesions, how and where do the intermediate groups with their highly descriptive names fit in? There is a resemblance between the contraction of the lower œsophagus and diffuse spasm in some of the examples which show large dilatations, and both groups have marked thickening of the walls. Furthermore, muscular hypertrophy is evident in some of the "curling" group, particularly in one œsophagus which came to excision and was subsequently included by Sloper in his paper on "Idiopathic diffuse muscular hypertrophy of the lower œsophagus". The radiographs of this patient also showed beads and curls, in fact, presented all abnormalities other than diffuse spasm.

From this evidence it is suggested that irregular contractions are associated with hypertrophy of muscle, which, if sufficiently widespread, may produce the picture of diffuse spasm. Furthermore, these records show that such abnormalities affect men of middle age who often suffer from other alimentary diseases such as peptic ulcer. Cardiospasm appears to be an entity quite different in its clinical, pathological and radiological pictures.

Occasionally one comes across a patient with dysphagia in whom the radiological changes are those of immature cardiospasm with little dilatation. As the years pass the condition remains stationary, and, at times, a resemblance to diffuse spasm may be observed (Fig. 6). On the other hand one long-standing case of cardiospasm was found to have gross dilatation

of the upper œsophagus, but the lower œsophagus was broken up into a chain of large balloons.

Rolleston in 1899 suggested that the variety of diffuse œsophageal hypertrophy might be an early and still fully compensated cardiospasm. Although I have hinted that these disorders may be related, the evidence presented indicates that neuromuscular lesions—despite the occasional similarity in the radiological changes of the initial stage—take two distinct forms, cardiospasm and diffuse spasm, and most of the curiosities which appear in the intermediate groups are manifestations of diffuse spasm.

Dr. R. E. Bonham-Carter: *On the Ætiology of Œsophageal Hiatus Hernia*

Barrett (1950) has done so much to clarify the muddled nomenclature of this condition that I must be careful not to remake confusion. He called the alimentary canal throughout the thorax the "gullet"; this tube could then consist of œsophagus or of the stomach. It is in this sense that the word "gullet" will be used.

May I first draw your attention to other hernias of gut from the peritoneal cavity. There are two common factors in their ætiology. The first factor is a hernial orifice which is too large. This may be so large that the peritoneal contents are never contained, or the orifice may become too large by the stretching of antonic muscles in age or illness. The second factor is stress. This stress, if sufficiently great, will cause herniation, proportionately more easily through larger orifices. The instances quoted include athletes, stevedores, and old folk with coughs. Why do some athletes, some stevedores and some old folk with cough herniate, while others do not? Is it because they are more energetic, lift heavier weights or have worse coughs? Or is it because their hernial orifices are larger than their fellows?

I have screened radiologically a large number of newborn babies. They come to me because they vomit or have suspected congenital heart disease. Some of both these groups have a free reflux from the infradiaphragmatic stomach in the gullet while supine. So free is this reflux at times that with a full stomach it occurs with each inspiration. In these there is no evidence of hiatus hernia, nor do all these babies vomit. The phenomenon appears temporary and if vomiting occurs it is improved by sitting the babies up. The frequency of this type of reflux in the newborn baby is not yet known. It appears, however, that some babies are born with temporarily incompetent lower ends to their gullets. It could be that this improvement was due to improvement in tone or an effect of growth upon a hernial orifice which was congenitally a little too large.

We are analysing 136 cases of œsophageal hiatus hernia in children seen at Great Ormond Street. The full analysis will be published later. All have been œsophagoscoped and fluoroscoped. There is a direct correlation between the findings at œsophagoscopy and fluoroscopy though these were not done by the same observers.

103 of these 136 patients had symptoms dating from the first week of life, suggesting a hernial orifice so large that the stomach is never contained below the diaphragm. Anatomists are silent about the size of this opening at varying ages. I can only say that in the 64 that have been operated upon it has appeared large, or large enough to contain liver.

In this group of 136 patients we have found 5 with genuine congenital hypertrophic pyloric stenosis proved at operation, all doubtful tumours being excluded. The incidence of congenital pyloric stenosis is 3·5 to 4 per 1,000 live births. Here we have 5 in 136 and Carré *et al.* (1952) found a comparable figure in their study of hiatus hernia in children. Thus we have a figure at least ten times the expected frequency of congenital pyloric stenosis. This makes one think of a causal relationship between hiatus hernia and congenital pyloric stenosis.

Also in this group of 136 there are a number of children with severe mental defect, 3 have sucrosuria, a syndrome described by Moncrieff and Wilkinson (1954), 2 have phenylketonuria and 1 has kernicterus. All those have biochemical associations if not excuses for their backwardness. In addition we have some children just as backward in this group but without such biochemical excuses, and have thought it wiser to exclude these for the sake of argument. The incidence of this relatively severe degree of mental defect is not greater than 1% of live births and the combined incidence of the biochemical association of the 6 described is one in many thousands of live births. Here we have 6 in 136, at least five times the expected incidence of severe mental defect. Again this indicates a causal relationship between hiatus hernia and mental defect.

The only relationship that I can see between severe mental defect and congenital pyloric stenosis is that they both vomit: the latter from intestinal obstruction and the former from inco-ordinate swallowing with choking and inco-ordinate peristalsis of the gullet, which we have seen in these patients.

This, therefore, is the hypothesis. Some babies, proportions as yet unknown, are born with large œsophageal hiatuses. Some of these are so large that the normal peritoneal contents are never contained. I believe this happened in at least 103 out of our 136 patients. In other newborn babies the hernial orifice appears to have been temporarily too large and either growth or an increase in muscle tone renders the lower end of this gullet competent again. In the third group the orifice remains a bit too large and if stress is applied herniation results.

The association of vomiting from other causes with hiatus hernia is well recognized; acquired pyloric stenosis, pregnancy and migraine are quoted. The conclusion is that the stress required to cause herniation in the third group is commonly vomiting.

I must apologize for indulging in so much speculation but I believe that œsophageal hiatus hernia is commonly due to an hiatus which is too large. This may be congenitally too large or become so with age or illness by atonicity. In those that are much too large the peritoneal contents are never normally contained. In those not quite so large stress is needed to cause herniation. This stress is commonly caused by vomiting.

My thanks are due to Professor R. S. Pilcher and Mr. D. J. Waterston, who did the œsophagoscopies, to Dr. J. Sutcliffe and Dr. J. W. Wells, who did the fluoroscopies and to Dr. Joyce Burke, who is helping us to analyse this series.

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Mr. A. Bowen-Davies said he was inclined to agree with Mr. Barrett that perforations of the œsophagus were occurring more commonly now than hitherto, and he believed one reason for it was modern anæsthesia. It did, of course, make the operation very much easier, but there was one great drawback in that, owing to depressed respiration, the œsophagus did not open itself up as it used to do, and so give a view down the œsophagus which showed whether the instrument was pointing in the right direction. Now one really had to force the walls apart, and in his view this had something to do with the increasing number of perforations which were occurring.

Dr. F. Avery Jones said he would like to mention two other unusual conditions of the œsophagus: one was the peptic œsophagitis which one could view post-operatively, and the other was the lesser degree of trauma of the normal œsophagus which one could get with vomiting. This could cause small longitudinal lacerations at the cardio-œsophageal junction as described by Mallory and Weiss some years ago and was the cause of hæmatemesis in patients who had vomiting from some other cause.

Mr. S. W. Allinson said that when he was a house surgeon about twenty-six years ago he was associated with an elderly patient who had difficulty in swallowing and epigastric pain. The person who was carrying out the examination in the X-ray Department noticed barium pass into the trachea through what was thought to be a fistula between the œsophagus and the trachea. The patient became very ill and died shortly afterwards.

A diagnosis of carcinoma of the œsophagus was made and the relatives were informed. However, it was later decided to hold a post-mortem examination and this was performed by Sir Bernard Spilsbury. The œsophagus was normal except for tightness of the upper end which he considered was due to ante-mortem or post-mortem spasm.

The **President** and **Mr. W. C. Gledhill** also took part in the discussion.

Mr. N. R. Barrett, in reply, said he was interested in Dr. Avery Jones' remarks about hæmatemesis with partial ruptures. Those cases might be fairly common and he could not see how one was to know unless one did an œsophagoscopy on all people who had a little bleeding after vomiting, but as it was possible to rupture a normal œsophagus with vomiting he did not think it very unlikely that minor degrees of trauma could occur.

Professor P. R. Allison, in reply to Mr. S. W. Allinson said it was well known that a debilitated patient, particularly after an operation, might inhale part of what he tried to swallow into his trachea. The investigation of such a possibility was better carried out with lipiodol rather than barium as it caused less trouble in the lungs.

How much spasm could occur *post mortem* in the œsophagus he did not know, but a whole book had been written about the movements of the œsophagus based on specimens that were not only dead but had been pickled in formalin for some weeks. Spasm was described in these specimens but it was difficult to say when it occurred.

Section of Odontology

President—Professor H. H. STONES, M.D., M.D.S., F.D.S. R.C.S.

[*November* 28, 1955]

The Isolation and Examination of Odontoblasts in the Fresh Unfixed State

By IVOR R. H. KRAMER, M.D.S., L.D.S. R.C.S.

*Department of Dental Pathology, Institute of Dental Surgery, Eastman Dental Hospital, Gray's Inn Road, W.C.*1

BECAUSE of their relationship to the hard, calcified dentine, odontoblasts are usually examined by means of stained decalcified sections. However, the processing of the tissues necessary for the preparation of such sections makes it almost inevitable that a certain amount of distortion of the cells will occur. It was thought likely, therefore, that if a method could be devised for the isolation of odontoblasts in the fresh unfixed state then a more true picture of their morphology would be obtained.

Method.—Normal premolars extracted for orthodontic purposes were used. Immediately after extraction under general anæsthesia, the teeth were placed in physiological saline and taken to the laboratory. With a diamond or Vulcarbo disc a shallow cut was made in the enamel of the mesial or distal surface, the cut running up to the occlusal fissure. With the tooth resting on a firm surface, a straight enamel chisel was placed in the cut and struck a sharp blow with a hammer. This split the tooth in two, the plane of cleavage passing through the pulp chamber. The half of the tooth containing the pulp was then taken, and with a fine scalpel the pulp was carefully peeled away from the dentine. Because of the mode of connexion of the odontoblasts to the dentine, it was assumed that this procedure would leave part of the odontoblast layer still attached to the hard tissue. With a sharp scalpel blade fine shavings of tissue were then pared away from the inner dentine surface, carrying with them some of the adherent odontoblasts. Throughout these manipulations the tissues were kept moist in physiological saline. When the shavings were obtained they were collected in a drop of saline on a slide, a coverslip was applied, and the specimen was ringed with a Vaselin-paraffin wax mixture to prevent evaporation. Phase contrast microscopy was then used to examine the preparation.

Whilst this technique was undoubtedly successful in giving a yield of isolated odontoblasts, it was found that they could not be distinguished with certainty from the other pulp cells that were present. Therefore, the final stages of the technique had to be altered, and instead of the shavings being taken parallel to the inner dentine surface, they were taken approximately at right angles to this surface.

This provided a number of slender dentine shavings in which the tubules were cut lengthwise, and where odontoblasts were adherent to these shavings they could be identified with certainty, for their dentinal processes could be seen entering the tubules in the hard tissue fragments.

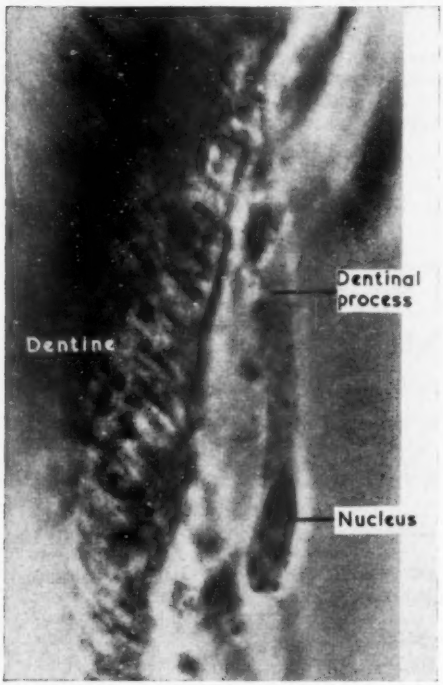

FIG. 1.

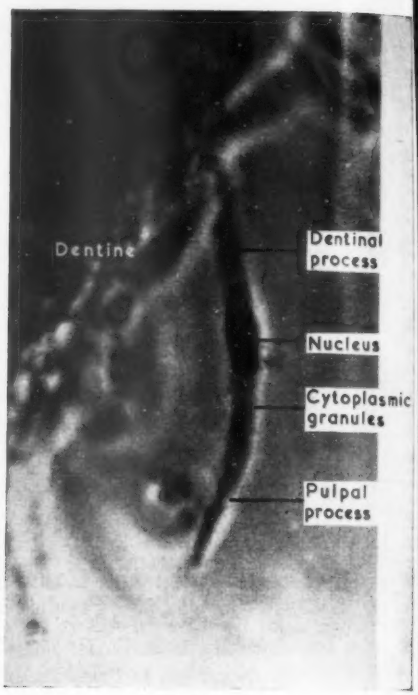

FIG. 2.

With practice, it was found that the preparations could be completed and under the phase contrast microscope within five to six minutes of the tooth being extracted. It was felt that the cells were unlikely to undergo serious morphological change in this time.

Results.—Figs. 1 and 2 show isolated fresh odontoblasts prepared by the method described. In each case, the dentinal process is probably pulled partially out of its normal position in the dentinal tubule. However, the processes are still clearly running into tubules, thus showing that the cells are odontoblasts. It will be seen that there is no evidence of any abrupt constriction of the cell where the process runs into the tubule, nor is there any evidence of adherence of the pulpo-dentinal membrane to the neck of the cell. In the cell shown in Fig. 1 a typical short pulpal process is seen.

[The communication was illustrated by a film showing the technique of the isolation of the cells and some of the results obtained.]

The Surgical Correction of Variations in the Facial Skeletal Pattern

By J. H. HOVELL, F.D.S., M.R.C.S., L.R.C.P.

IN this paper I have endeavoured to bring together and classify in an orderly manner the variations of the facial skeleton, which are susceptible to surgical correction, describe as far as possible the various methods of treating these variations and give my own personal views arising from my own experience in their treatment. Assessment is naturally limited by the relatively small number of these cases coming to one individual.

Classification.—Table I shows the classification I have adopted for abnormalities of the

TABLE I.—CLASSIFICATION OF VARIATIONS OF THE FACIAL SKELETON

I. Variations of normal type but excessive degree.
   (*a*) Skeletal Class III
   (*b*) Skeletal Class II
      (i) Superior protrusion
      (ii) Inferior retrusion.

II. Variations of abnormal type.
   (*a*) Prenatally determined growth dysplasias
      (i) Cleft palate
      (ii) Underdevelopment of maxillary complex } Maxillary
      (iii) Oxycephaly
      Mandibular agenesis. Mandibular
   (*b*) Natally or postnatally determined growth dysplasias
      (i) Maxillary
      (ii) Mandibular.

facial skeletal pattern. In orthodontic treatment one is now accustomed to assessing the basic skeletal pattern when making a diagnosis. Angle's three classes are well known. As a result of cephalometric appraisal of the results of orthodontic treatment it is now appreciated that all that can be done by the orthodontist is to change the positions and axial inclinations of the teeth within the dental base relationship and skeletal pattern provided by heredity.

The more severe degrees of variation in the skeletal pattern are such that the teeth cannot be moved by orthodontic treatment into normal or even good functional relationship. Surgical correction or adaptation of the skeletal pattern is the only treatment possible in these cases. There is an intermediate zone in which, though orthodontic treatment is possible, the results are æsthetically unpleasing and the teeth are in poor functional relationship. Thus there are good reasons for not undertaking orthodontic treatment for this type of case, with a view to surgical correction of the deformity if desired by the patient at a later date.

The first group of cases is that in which those variations of skeletal pattern seen daily by the orthodontist are present in abnormal degree.

The second group consists of those abnormalities of skeletal pattern which are completely outside the range of normal variations, and which I have further subdivided into those arising prenatally and those arising postnatally.

Skeletal Class III.—Although generally referred to as mandibular prognathism, this is in fact associated in a large number of cases with some degree of maxillary underdevelopment. From the point of view of treatment this can be ignored, as very good results, both cosmetic and functional, are obtained by treating the mandible only. The essential of treatment is alteration of the mandibular configuration, so that the lower incisors are brought back into correct relationship with the uppers. There are two main groups of methods of doing this. The first consists of sliding osteotomies of the ascending ramus, the second of bilateral resection of some part of the body.

Sliding osteotomies of the ascending ramus can be done either blind or under direct vision. Of the blind approaches, the best known is the method of Kostecka using a Gigli saw to divide the ascending ramus. The Swedish blind approach employs a small incision behind the posterior margin of the mandible, which is approached by blunt dissection owing to the proximity of the facial nerve. The mandibular vessels and nerve are guarded by a flat instrument passed on the lingual side between them and the ascending ramus. The line of this instrument also helps to act as a guide for the line of section of the jaw. This line of section is most important and must be carefully planned pre-operatively from the study of models and cephalometric lateral radiographs, so that as the anterior fragment is moved distally the bone ends remain in contact and neither separate nor overlap. Where possible the bone section should be made in such a way that the resulting fracture is a favourable one, hindering forward and medial displacement of the posterior fragment. The section must be above the level of the mandibular foramen, and it is surprising how little ascending ramus is available between this and the sigmoid notch.

The third blind approach is the intra-oral approach to the front of the ascending ramus, which is divided by a saw. Some surgeons use an osteotome to complete the division, but in my hands this has not proved a success, as even with preliminary sawing, spicules of bone are left which prevent accurate apposition of bone ends. I do not favour the intra-

oral approach, for I do not consider the availability of antibiotics any excuse for introducing infection into a fracture line in the absence of any other reason for so doing.

In the pre-operative planning for these cases it is usually found that the desired occlusion of the teeth can be obtained without any preliminary adjustments; on occasion, however, pre-operative orthodontic treatment or adjustment by stoning may be necessary.

When good occlusion cannot be obtained without considerable adjustment, the alternative of a body resection should be considered.

In performing a sliding osteotomy under direct vision, the main principles of the operation are the same. Careful pre-operative planning of the direction of the section is necessary. The approach can be either via an incision extending from just below the facial nerve downwards behind and below the angle, or via a higher incision across the course of the facial, the mandible being reached by blunt dissection.

In either case the ramus is divided under direct vision and the bone ends wired into good apposition. A single wire is all that is necessary to prevent forward or medial displacement of the posterior fragment.

The holes for wiring should be drilled and wire threaded on the posterior fragment before division of the ramus is complete, so a bit of extra pre-operative planning is necessary here to determine exactly their correct relative positions antero-posteriorly on proximal and distal fragments. If the holes are incorrectly placed the wire will, of course, produce displacement instead of apposition.

Immobilization of the distal fragment is effected after complete closure of the wounds. Some operators believe that union is accelerated in these cases by insertion of bone chips around the fracture line and in any spaces present between the bone ends. Cancellous iliac crest bone is used. I have used this procedure myself, but not sufficiently often to be able to draw any conclusions from the results obtained.

Body resections can be performed either in the space provided by a missing or extracted tooth or teeth, or nearer the angle behind the last tooth. Very careful pre-operative planning must be undertaken to determine the size and shape of the portion of bone to be removed, as there is even less error permissible in this operation than in the sliding osteotomy. Also, the size and shape of the segment of bone to be removed having been determined, some method must be adopted for outlining this at the actual time of operation. The construction of templates is one method used: this has the disadvantage that slight misplacement at the time of section may result in the division of the root of a tooth—a most unwelcome complication.

I have devised a method using pins slotted into the cap splints, which are set to run along the line of section, and can be used as an actual physical guide to the saw, which much facilitates sawing. Radiographs are taken in the planning stage to ensure that the pins do not cross the root of a tooth (Fig. 1, *see* p. 551). This method is only available when there are teeth on both fragments. If there are teeth on the anterior fragment only, one pin can be used to give the line of the anterior cut in conjunction with a template for the posterior cut, except in those cases where it is hoped to avoid entering the mouth, in which case a template only can be used, or a two-stage operation performed.

There are two main categories of body resection, one-stage and two-stage operations. The one-stage operation when carried out in the centre portion of the body of the mandible necessitates opening the fracture line into the mouth. The actual site of section must be governed by the best resultant final occlusion to be obtained according to the site of section, and is also affected by the position of any pre-existing spaces in the dental arch. The most commonly missing teeth are the first permanent molars and section in this region usually gives an excellent occlusal result. If the gap provided by one tooth is not large enough, further extraction, usually a second premolar, may be necessary. Section at this site has the added advantage of leaving undisturbed the attachments of the elevator muscles of the jaw.

It is highly desirable that the integrity of the mandibular nerve be preserved during the section of the jaw. In a number of my earlier cases, I omitted to do this. Sensation invariably recovered, but two of them were left with a persistent causalgia. Fortunately, it is a simple, though laborious matter, to expose the nerve and lift it from its canal before sectioning the bone. Personally I remove it as far forward as the mental foramen and hook it over the guide pins, which keep it well clear of the operative field when sectioning the bone. Following this, there is nearly always transient anæsthesia from the unavoidable handling of the nerve, but this soon recovers.

Holes are drilled for lower border wires on both sides before any of the sectioning cuts are carried to completion.

Having completed the section, a not too tight lower border wire is placed on each side and the fragments then immobilized to the upper by means of the re-placed cap splints, by means of wiring between hooks. After three to five weeks union is usually sufficiently firm to permit fixation of the fracture by localization across the fracture line so that intermaxillary fixation can be removed. It is my custom to dispense with complete intermaxillary fixation as soon as possible to permit mastication, and to maintain it if necessary at times other than meals by elastics, which can be removed by the patient for eating.

Experiments were made with L-shaped sections, to bring larger areas of bone-end into apposition. These were abandoned for three reasons:

(1) They considerably increased the difficulty and duration of the operation.
(2) There was no apparent reduction in the time required for union.
(3) If the section is not parallel-sided, and it seldom is, the limbs of the Ls do not fit snugly and bone apposition is actually reduced.

The two-stage operation has as its objective the completion of the section in a sterile field without entering the mouth. The basic principles and pre-operative planning are exactly the same as in the one-stage section. In the first-stage bone is removed as far down as the mandibular canal. Care must be taken that the removal is complete on the lingual aspect. I use the same method of guide pins for showing the line of section, and at the first stage cut grooves on the outer surface of the mandible towards the lower border along the required line of section, as these pins coming through from the mouth obviously cannot be used in the second stage.

At the second stage, carried out when healing is complete, the nerve is exposed and freed as in the previous operation and the section completed. The advantages are obvious. The fracture line is uninfected and bone chips can be used if required to hasten union.

Choice of operation (Fig. 2, *see* pp. 552–553).—Having described the main principles of the types of operation available for the correction of this deformity, it is a matter of great importance that the diagnostic, ætiological and physiological criteria which determine the choice of operation, should be considered.

The first reductions of mandibular prognathism which I did alone or in conjunction with a plastic surgeon were blind ascending ramus osteotomies either by the Swedish or Kostecka method. The results varied from first class to appalling. In no case was it possible to remove intermaxillary fixation in under twelve weeks, and in one case elastic traction between meals had to be continued for almost a year.

An analysis of these cases showed two main reasons for delay in union or a poor occlusal and æsthetic result. The first and obvious one was tilting of the small posterior fragment out of contact with the anterior fragment. The second was the presence of some degree of anterior open bite before treatment.

I can see no sure way of getting 100% apposition of the bone-ends in an ascending ramus osteotomy, with its associated disturbance of muscular balance, other than by sectioning and fixing the fragments under direct vision. This also permits the insertion of bone chips, and is the method I now employ via the post-mandibular approach.

The blind approach increases the hazard of hæmorrhage and the difficulty of its control. In one of my cases a large hæmatoma developed. Death due to respiratory obstruction as a result of hæmorrhage from a divided mandibular artery has occurred in another case. For these reasons, I personally would not now consider a blind ascending ramus sliding osteotomy to be good surgery.

When an ascending ramus slide is performed on a case of anterior open bite, as the anterior fragment is displaced backwards the incisor teeth tend to become further separated in a vertical plane. This separation is not a small thing which can be overcome by force at the time of operation or by elastic traction from splints afterwards. The usual result of force applied at operation is the avulsion of the splints from the teeth. Elastic traction after operation is probably the easiest way of slow and comparatively painless extraction of the teeth. I think this inability to reduce an anterior open bite is due to the spheno-mandibular ligament, whose normal function is to prevent downward movement of the lingula during masticatory movements.

The relapse to an anterior open bite which may occur if union is delayed or fixation is removed too soon is due to a different cause. It is, I think, muscular imbalance and due to the pull of the internal pterygoid upon the backwardly displaced ascending ramus. This question of muscular imbalance is, I think, a most important one. The words of a well-known orthopædic surgeon with whom I discussed this question were, "If you're fighting

muscle, you must look out for trouble". I do not think it possible permanently to stretch muscles, and if an elevator, for example the internal pterygoid, is stretched as must be the case in many ascending ramus slides either it will produce a relapse or retention must be maintained until there is actual shift of the muscle attachment. We know that this type of shift occurs during growth and I think that it happens after ascending ramus slides. But it takes time, and is another reason why prolonged retention may be necessary in these cases. Using the open approach, I find no difficulty in stripping the attachment of the internal pterygoid, and thus facilitating its reattachment in a new position.

To sum up, the degree of incisor overlap should be correlated with the amount of distal displacement required, and if there is any fear of an anterior open bite developing, a body resection is the operation of choice. When an anterior open bite is already present, an ascending ramus slide is definitely contra-indicated.

A further influence of soft tissue patterning has to be considered, and that is its relation to the axial inclination of the lower incisors. As a result of the recent work of Rix, Ballard and Gwynne-Evans, it is now well established that the position of the crowns of the teeth, in a labio-lingual and bucco-lingual direction, is determined mainly by their soft tissue environment. The lower incisors in Class III cases are usually severely retroclined. After operation, whether ascending ramus or body, the lower lip tension is reduced and the pressure from the tongue, which usually cannot be displaced back as far as the labial segment, is increased. The lower incisors, therefore, gradually become more upright and some degree of apparent relapse is produced, which, however, is entirely dental and not skeletal. This change in incisor inclinations is usually greater in body resections than in ascending ramus slides and must be allowed for in the pre-operative planning.

Open operation either on the ramus or the body, though not technically difficult, is laborious and time consuming. Plastic surgeons, who turn over the post-operative care of their cases to their dental colleagues, are particularly prone to fight shy of these procedures. Under the conditions provided by modern anæsthesia, the question of time and labour should have little or no influence upon the choice of surgical procedure to be adopted.

There is one more point to be mentioned. That is the question of the excessive bag of soft tissue which often remains below the mandible. In performing body resections I have recently joined my two incisions and excised a wedge of skin and subcutaneous tissue. The result is excellent, the bag is obliterated and the scar line tucks up into an invisible position under the jaw (Fig. 3, *see* p. 554).

Skeletal Class II facial bony patterns.—These much less frequently demand surgical correction for a number of reasons. First, tilting of the teeth by orthodontic treatment does much to rectify the appearance. Second, patients do not seem to mind their receding chins and seldom ask for, or even accept, the idea of surgical correction. Thirdly, the occlusion of the cheek teeth is often good, and a purely cosmetic operation, such as a bone graft to the chin, may be the better line of treatment.

There is a small residue of patients in whom correction or improvement of the skeletal deformity is the correct line of treatment. While in mandibular prognathism the associated small maxilla can usually be ignored, a Class II skeletal pattern may be due almost entirely to maxillary prognathism, and this factor must be taken into consideration. In some of these cases, masking the maxillary prognathism by bringing forward the mandible to an equal extent would produce a total facial prognathism so extreme as to be almost grotesque. In theory, the correct procedure is a maxillary resection, removing a segment of bone in the first and second premolar regions and setting back the incisors and canines. In practice, this is a very difficult procedure, both from the point of view of planning and execution, involving as it does section of the palate, nasal septum and outer surface of maxilla. It is difficult, in fact impossible, to plan a section which is not wedge-shaped and, therefore, would produce tilting and downward displacement of the labial segment, with increase in the overbite which is usually already excessive. In addition, the maxillary antrum is opened. Taking all these facts into consideration, I have yet to see a case in which I felt that such a procedure is justified. The alternative of removal of teeth and alveolectomy, either alone or in conjunction with a mandibular osteotomy or chin graft, being considered the correct line of treatment.

If an osteotomy is planned, again it may be in body, angle or ascending ramus. The last is the only one of which I have personal experience, doing a forward slide via a direct approach (Fig. 4, *see* p. 554). The same pre-operative planning is necessary as for a backward slide, and the technique is identical. Post-operative union appears to be more rapid and there is no tendency to anterior open bite.

Kazanjian and others describe an L-shaped slide in the centre of the body. From my own experience in this field the main difficulty, and the reason I did not adopt this method, would appear to be in finding adequate mucous membrane cover for the lengthened bone.

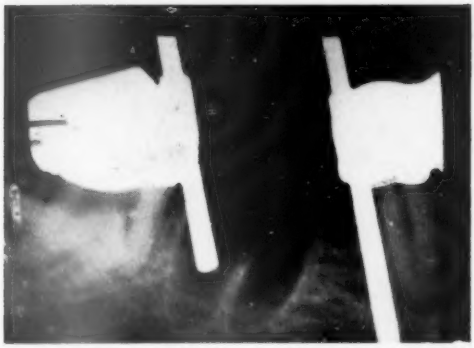

FIG. 1.—Radiograph of pins in position to show line of section clearing tooth-roots.

Fickling has developed an L-slide in the region of the angle, which appears to give excellent results and may well prove to be the operation of choice. It is not necessary to open into the mouth, so that chips can be used to build up the defect produced, and access is easy.

Skeletal anterior open bite.—This is the last excessive normal variation. There are two fairly clearly defined types of anterior open bite. The first and commonest, which is usually confined to the labial segments, is due to an abnormal behaviour pattern of the oro-facial musculature. There is an atypical swallowing action with anterior tongue thrust which prevents normal eruption of the labial segments. Surgery is neither necessary nor successful in these cases.

The second type of anterior open bite is due entirely to a skeletal deformity. There is a high gonial and Frankfort-mandibular plane angle and often a reduction in size of the maxilla. The skeletal bases are so widely separated in the vertical plane that the teeth fail to erupt into occlusion, not only in the labial segments, but also in the buccal segments, sometimes as far back as the last erupted tooth, so that only four teeth are in occlusion.

The remarks regarding open bite made in discussing mandibular prognathism apply here. Section should be below the mandibular foramen. If only the posterior teeth are in occlusion it can be at the angle, a slide being planned to allow rotation of the mandible around these teeth.

Usually, however, an antero-posterior discrepancy must be corrected as well as the anterior open bite, in which case a body resection immediately in front of the last occluding tooth is the best. The technique of the operation and pre-operative planning are as in the reduction of a mandibular prognathism, which indeed may also be present, and results in a wedge-shaped piece of bone being removed. Not infrequently, although bone has to be removed from the upper border, a defect is left at the lower border, and in some cases it may be found unnecessary to remove any bone but merely to create a triangular defect as the anterior fragment is swung upwards. The operation must, therefore, be performed without entering the mouth, in two stages if necessary, in order that this defect may be filled with bone chips.

Another factor which must be watched for, in case it produces relapse, is a large tongue. This is invariably present in anterior open bites due to endocrine dysfunction, in which I consider it is probably the main ætiological factor, but may also be associated with a skeletal open bite. Watkin and Sutton-Taylor have described cases in which partial glossectomy has been performed to eliminate this cause of relapse.

VARIATIONS OF SKELETAL PATTERN OF ABNORMAL TYPE [SUMMARIZED]

A. *Present Pre-natally*

(i) Cleft palate: The main procedure carried out by the oral surgeon is a mid-line maxillary osteotomy to widen the dental arch. The central defect may be left or filled with a pedicle graft and bone chips. This is most valuable in order to provide adequate retention for a stable full denture in later life and must be done while there are still an adequate number of teeth standing for splinting and fixation (Fig. 5, *see* p. 555).

(ii) Cleido-cranial dysostosis, oxycephaly, Treacher Collins syndrome: Treatment mainly by masking operations. Though more radical surgical procedures have been undertaken, their value is doubtful.

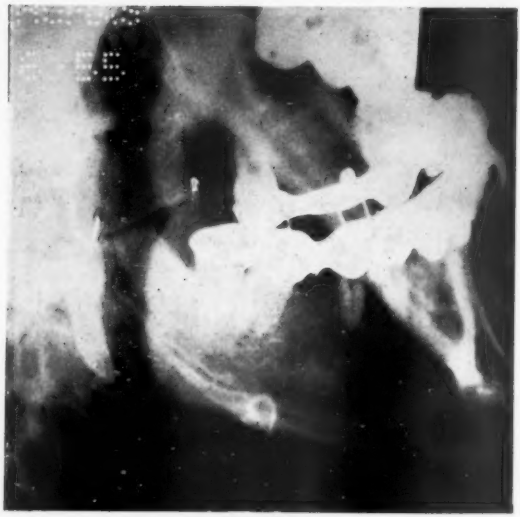

FIG. 2A.

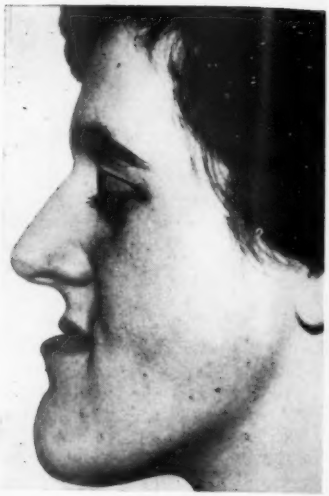

FIG. 2B.

FIG. 2.—A: Radiograph showing backward ascending ramus slide. B and C: Pre- and post-operative photographs of ascending ramus slide. D: Oblique lateral radiograph of body resection. E and F: Pre- and post-operative photograph of body resection.

(iii) Mandibular agenesis: Treatment now being explored is by serial bone grafts to the angle and ascending ramus during the growth period (Fig. 6, *see* pp. 555–556). Careful pre-operative planning, often involving orthodontic treatment, is essential, as also is post-operative control to permit eruption of the cheek teeth into occlusion and prevent relapse. The ultimate benefit accruing from this procedure as opposed to masking is still in doubt. My own view is that when the first arch agenesis affects the soft tissues equally with the bone, any attempt to lengthen the latter during the growth period is bound to relapse owing to the effect of the unchanged soft tissues. Only when the main defect is bony are early surgical procedures likely to be of any help.

B. *Arising at Birth or Post-natally*

(i) Maxillary underdevelopment: Treatment usually by masking operations and falls into the sphere of plastic rather than oral surgery. Its origin may be

(*a*) Infective.

(*b*) Traumatic—accidents or surgical trauma.

(*c*) X-ray damage to growth.

(ii) Mandibular underdevelopment due to natal or post-natal injury to the condylar growth centre. This may be due to trauma or infection, and is often associated with limitation of movement or even complete ankylosis of the temporo-mandibular joint. Serial bone-grafting as described for post-arch dysplasia is the ideal line of treatment in these cases, as the soft tissues are potentially normal.

(iii) Condylar hyperplasia: This results in overgrowth of one side of the mandible. Condylectomy may be necessary in severe cases. If growth ceases, surgical correction of the overgrowth by local procedures—sliding osteotomies, body resections and lower border trimming may be all that is necessary (Fig. 7, *see* p. 556).

It is important to realize that condylectomy not only stops the growth, but also corrects a great deal of the deformity, without as so often occurs in the normal mandible producing dysfunction of the opposite joint and reduced masticatory efficiency.

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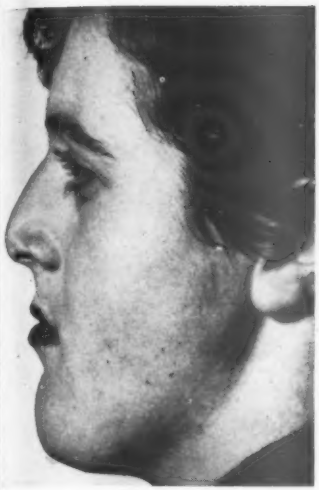


FIG. 2C.

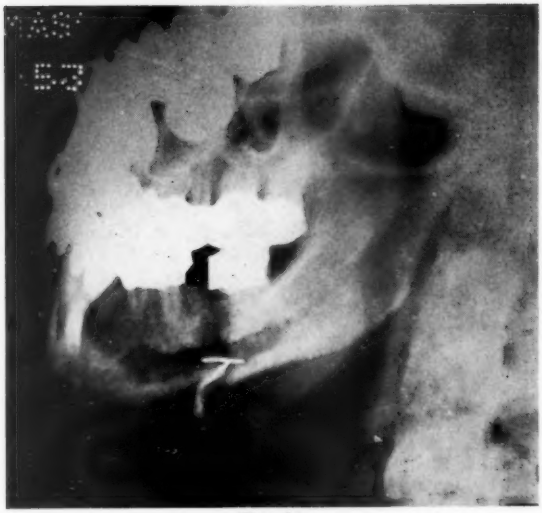


FIG. 2D.

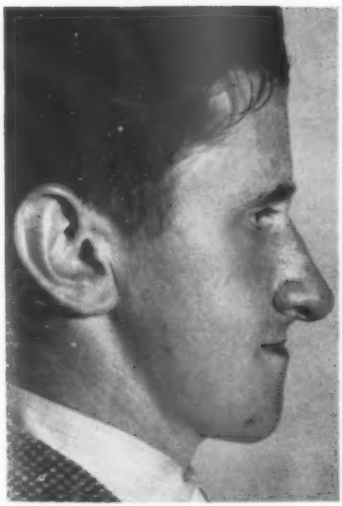


FIG. 2E.

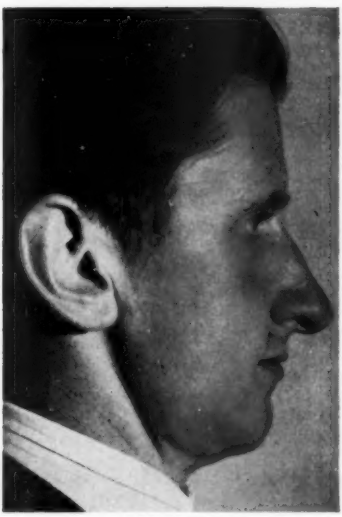


FIG. 2F.

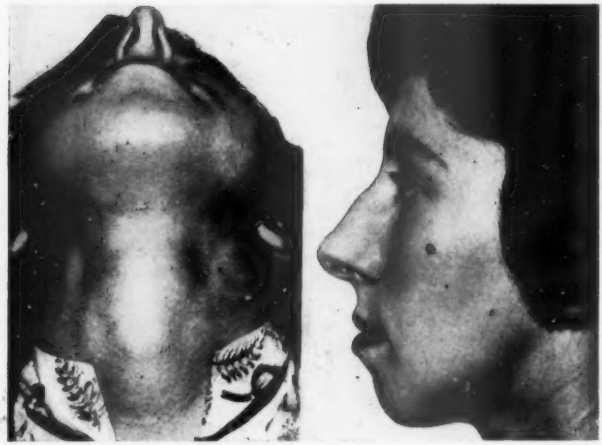


FIG. 3.—Result of excision of wedge of skin and soft tissue to remove submandibular "bag".

FIG. 4.—Radiograph showing forward ascending ramus slide.

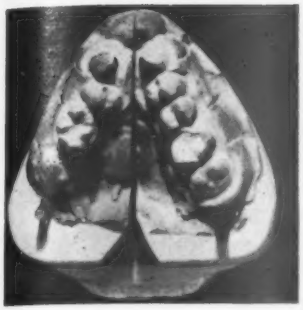


FIG. 5A.

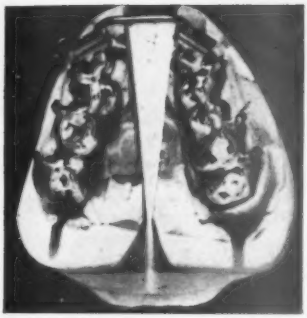


FIG. 5B.

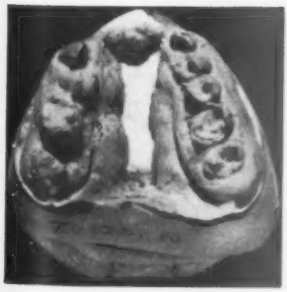


FIG. 5C.

FIG. 5.—Method of planning, construction of upper splint and post-operative result of a maxillary osteotomy.

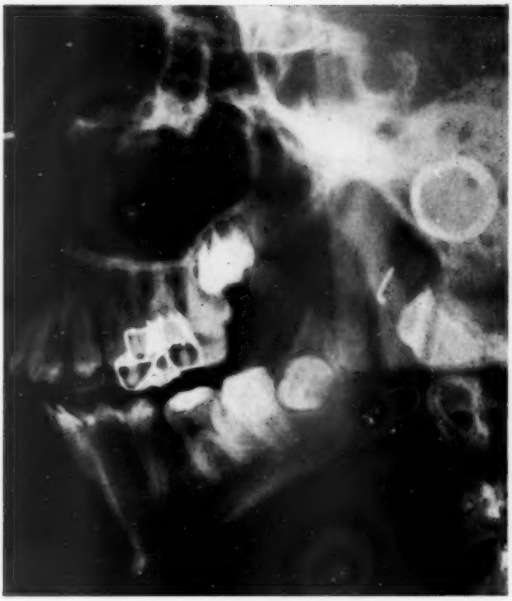


FIG. 6A.

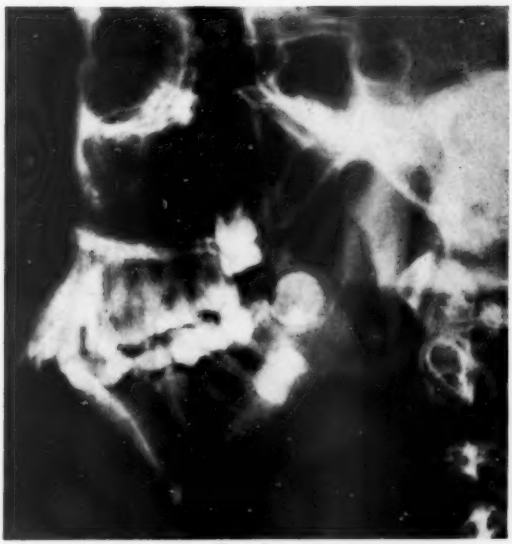


FIG. 6B.

FIG. 6.—Radiographs of mandibular agenesis (traumatic). A: Before. B and C: After correction by iliac crest graft to ascending ramus. (*See over* for Fig. 6C.)

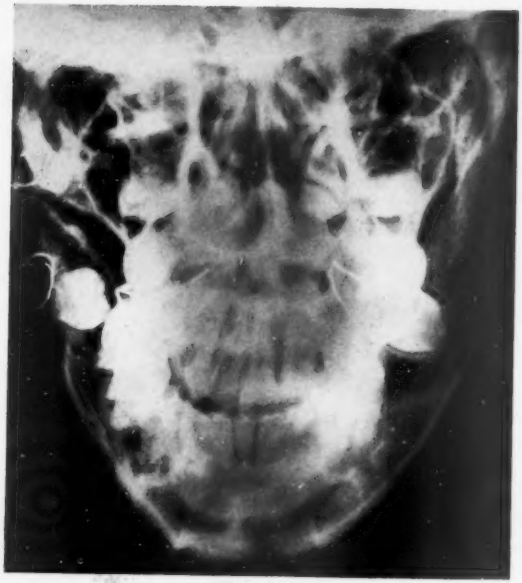


FIG. 6C.

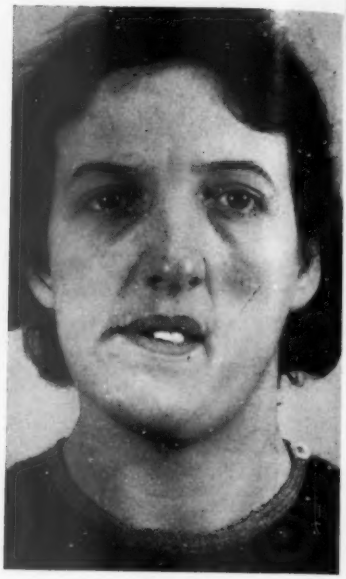


FIG. 7B.

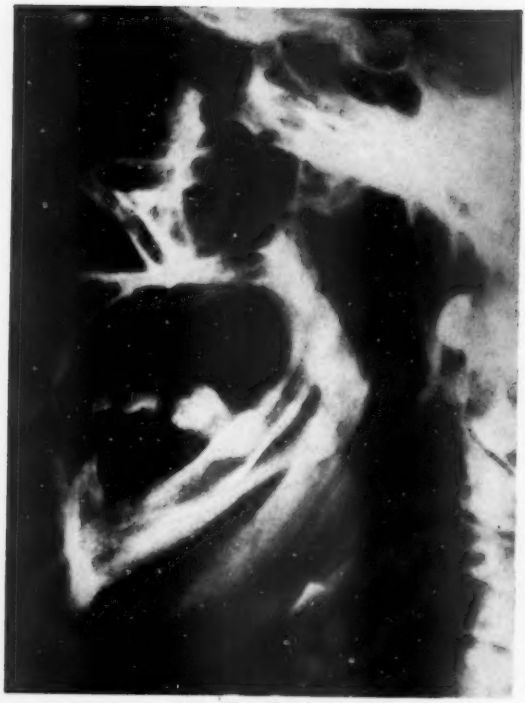


FIG. 7A.

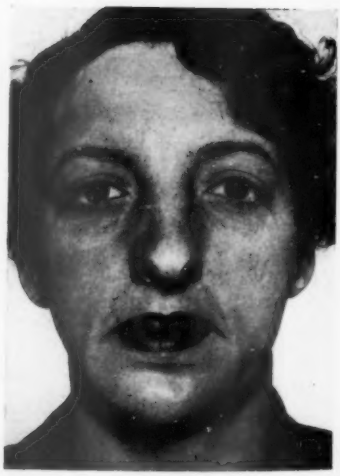


FIG. 7C.

FIG. 7.—Condylar hyperplasia. A: Radiograph. B: Pre-operative photograph. C: Post-operative photograph.

Section of Radiology

President—E. ROHAN WILLIAMS, M.D., F.R.C.P., F.F.R., D.M.R.E.

[*January* 20, 1956]

DISCUSSION ON THE CLINICAL AND RADIOLOGICAL ASPECTS OF DISEASES OF THE MAJOR ARTERIES

Mr. H. H. G. Eastcott:

We have in the past five years at St. Mary's Hospital seen examples of most kinds of arterial disease. Arteriography has been of the greatest help in planning their treatment, and indeed many of the present generation of surgeons have formed their ideas of these diseases from their X-ray appearances, for these have given clinicians their first accurate information about the structural and dynamic changes in the earlier stages before operation, amputation, or the autopsy room which show the conditions only in their more advanced forms.

With all this there is, as in other specialties which the radiologist has opened up for the surgeon, a risk of operating on the X-ray films, as it were, rather than the patient. I shall, therefore, describe some clinical problems which have not run quite true to type.

Gangrene of the Foot

This depressingly common condition is usually due to atheromatous disease and spreading thrombosis of the main artery to the part, as arteriograms will readily show, but in the following patients the main artery was patent well down into the limb yet ischæmic gangrene developed.

Case I.—A man of 45 developed a painful, congested foot and later necrosis of the toes. The popliteal pulse was strong and the arteriogram showed that the upper tibial vessels filled normally. A below-knee amputation should have succeeded. It did not heal, however, and the reason was that this patient's arterial obliteration affected small vessels only, for he was a case of thrombo-angiitis obliterans, as was later proved by the examination of the specimen.

Case II.—A woman of 60 with gangrene of the toes but vigorous pulses at the ankle. This was among the conditions originally described by Raynaud. It responds well to sympathectomy and local amputation, unless the patient is diabetic in which case the gangrene is a result of neuropathy, one evidence of which is the low intensity of the pain.

Case III.—A woman of 60 was in failing health. First one leg then the other became swollen and painful and moist gangrene developed in the feet (Fig. 1). It was noticed that the part was not cold, but hot; the pulses were obscured by œdema; arteriography, and later, pathological examination, showed all the arteries to be patent. This patient had venous gangrene; a spreading thrombophlebitis affected almost the whole venous system of the lower limbs and its effect was to strangulate them, producing the signs described in the process. She was found at autopsy to have secondary carcinoma in the liver.

Case IV.—A woman of 40 with mitral stenosis developed acute ischæmia of the lower calf and foot. A bounding popliteal pulse was present. Her husband attempted to warm the foot with a hot-water bottle and though it was not excessively hot, the area in contact with it developed full thickness necrosis. This gangrene was due to the increased metabolic needs of warmed tissues lacking a blood supply, and the popliteal pulse was that commonly felt just above the site of impaction of an embolus, at the bifurcation of the artery.

Aortic Aneurysms

In the thoracic aorta aneurysm formation is due to syphilitic aortitis or to coarctation of the aorta with post-stenotic dilatation. The latter type does not as a rule produce any special symptoms other than those of the coarctation and is discovered only at operation. Aortography has been of value in these cases, for it reveals the complication before operation so that arrangements can be made for grafting the considerable defect in the aorta after excision of the lesion.

Syphilitic aneurysms of the aorta occur in middle-aged or even younger men.

Case V.—A man of 35 experienced backache, and when erosion was seen, in lateral X-rays, of the bodies of the vertebræ of the lumbo-dorsal junction he was treated elsewhere as a case of Pott's disease until aspiration of a suspected abscess yielded arterial blood under pressure. There was no abdominal swelling. He was transferred to the Surgical Unit at St. Mary's Hospital and was treated by grafting under hypothermia. Even with this precaution he developed temporary spinal cord disturbances from the aortic clamping and the division of several intercostal arteries.

Arteriosclerotic aneurysms affect the abdominal aorta below the renal arteries, and patients are generally over 60. Rupture follows within weeks or months of the first abdominal pain, and the mortality of this complication in the writer's experience is 100

FIG. 1 (*Case III*).—Venous gangrene.

FIG. 2.—The thrombus from the aneurysm of *Case VI*, showing the small size of the channel → relative to the sac.

per cent. On the other hand the chances of cure with resection and grafting of the aortic bifurcation are good in our experience, though the late results have yet to be seen.

Case VI.—This man of 65 with increasing abdominal pain for some months was found to have a pulsatile abdominal mass. The aortogram confirmed the diagnosis of aortic aneurysm but did not suggest that the sac was large. The reason for this was evident at operation when a huge tubular thrombus was found within the sac (Fig. 2); the contrast medium had not filled more than the central channel. Reconstruction in this case was with an orlon cloth bifurcation and the patient has been back at work for more than a year.

An aneurysm may leak rather than burst, and unusual clinical appearances are sometimes encountered.

Case VII.—In this patient a saccular aneurysm leaked behind the peritoneum and compressed the iliac vessels on the left side, producing acute ischæmia of the limb. Rectal examination confirmed the presence of a large hæmatoma, which was also seen in the cystogram to be occupying nearly a half of the pelvis. In this case operative evacuation of the clot, and reconstruction of the aorta with a homograft was undertaken, within twenty-four hours of the disappearance of the pulses, and a normal blood flow was re-established.

Not all aneurysms are the cause of the patient's symptoms. Generalized arteriosclerosis may involve aneurysm formation in some places and atheromatous occlusion in others.

Case VIII.—A man of 58 with a fusiform aneurysm in each common femoral artery had no pulsation in either limb below this point. He eventually required an above-knee amputation on each side for pain and distal gangrene.

Aortic Thrombosis

Insidious thrombosis appears to begin in relatively young patients and first involves the proximal portion of the common iliac arteries, later progressing to a total aortic occlusion. Such patients have fairly severe intermittent claudication, affecting the buttocks as well as the lower limbs. Gangrene is usually long delayed.

Case IX.—A woman of 39 became completely crippled with intermittent claudication. There were no pulses below the epigastrium. There was evidence of commencing renal failure, and at operation under hypothermia the aorta was seen to be occluded up to and into the left renal artery. A homograft was substituted for the aorta below this level, and its iliac branches, and the patient remains well and active over three years later.

Arterial Injuries

Apart from fatal hæmorrhage, the complication most to be feared is that of gangrene of the part supplied by the divided main artery. We have repaired several common femoral arteries, either by anastomosing or grafting the ends forming the gap. Surgical mishaps in hernia or varicose vein operations have sometimes brought these patients to us, and also the bizarre accident, first described by Jaboulay in 1892, in which a butcher severs his own right femoral or external iliac artery with a knife.

Case X.—This butcher aged 19 was killing a pig when it escaped and the knife passed through the femoral artery above and below the profunda branch. The hæmorrhage had been controlled first by pressure and then by arterial ligation. He was then referred for emergency grafting and the two homografts functioned well.

There have also been 3 cases of axillary or brachial artery laceration by a fracture of the humerus. The tendency of such patients to develop lasting ischæmic effects may be due to the damage done to the available collateral channels by the soft tissue injury. It has been found to be well worth while reconstructing this injured vessel, in 2 cases by direct anastomosis, and in the other by homograft.

Acknowledgment.—I am indebted to Dr. R. D. Green for permission to publish Case III.

Dr. David Sutton (St. Mary's Hospital, London):

My contribution is concerned largely with the radiological problems both in technique and in diagnosis presented by the lesions under discussion.

At St. Mary's Hospital all our angiographic investigations are carried out in the X-ray department and by the radiologists. We rely entirely on percutaneous techniques, and these are carried out with few exceptions under local anæsthesia and basal narcosis only. Arteriography performed in the operating theatre under general anæsthesia and by open operation should be regarded as both antiquated and unnecessary, and is often technically unsatisfactory. Two basic methods are used: (1) Percutaneous needle puncture. (2) Percutaneous arterial catheterization.

Percutaneous needle puncture can be carried out on most of the major vessels in the body. Table I (p. 561) shows the details concerning needle puncture of individual vessels as personally practised.

Where simple percutaneous needle puncture provides a ready answer to the problem under investigation this has been the method used. In certain other cases, and in particular when dealing with lesions involving the intrathoracic aorta and great vessels or the upper abdominal aorta, we have used the ingenious method of percutaneous arterial catheterization devised by Seldinger of Stockholm. In addition to catheterizing the abdominal aorta and iliac vessels from the femoral artery as originally suggested by Seldinger himself, we have also used his technique for catheterizing the thoracic aorta from the carotid artery (Sutton, 1955–56). We have occasionally also been using this technique of percutaneous carotid catheterization for cerebral angiography as routinely practised by Liverud of Oslo.

Table II (p. 561) gives details of the different areas which can be investigated by percutaneous catheterization.

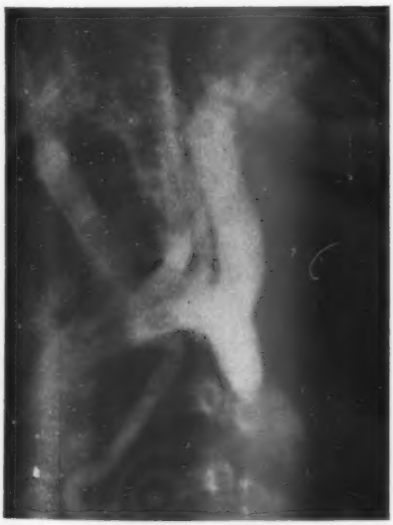


FIG. 1.—Coarctation of aorta shown by percutaneous trans-carotid catheterization.

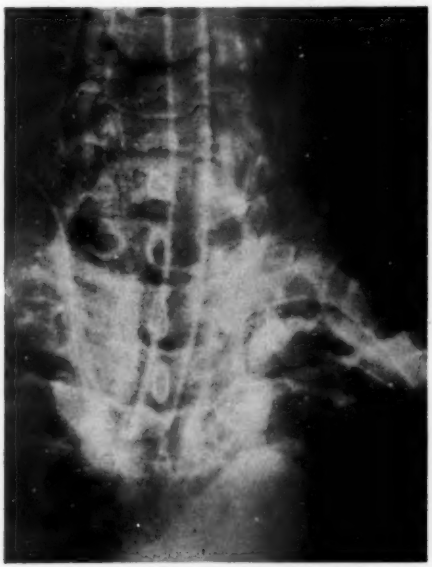
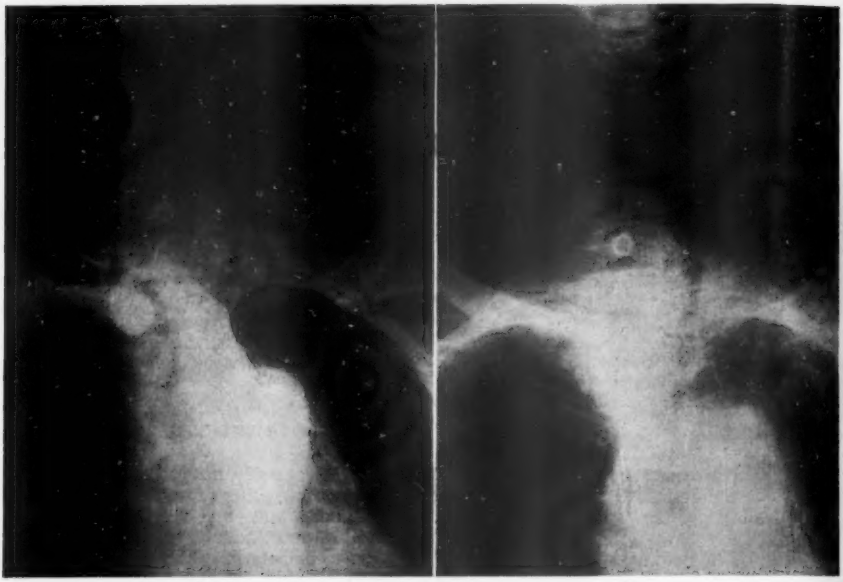


FIG. 2.—Thrombosis of left common carotid artery in the thorax. The left subclavian and vertebral arteries are filling well as are anastomotic vessels in the neck.



A B

FIG. 3A and B.—Thrombosis of left subclavian artery. The origin of the left carotid artery is also stenosed giving rise to delayed filling. Note the aneurysm of the innominate artery.

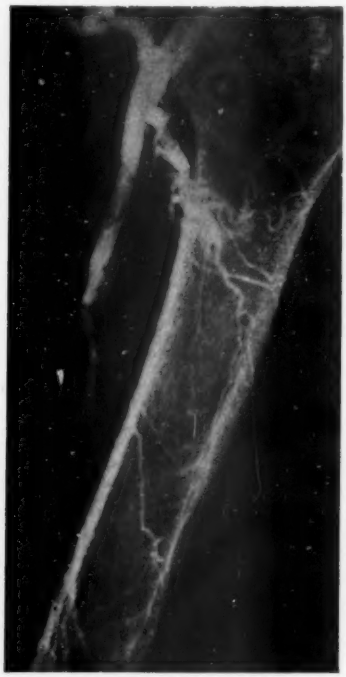


FIG. 4.—Thrombosis of brachial artery.

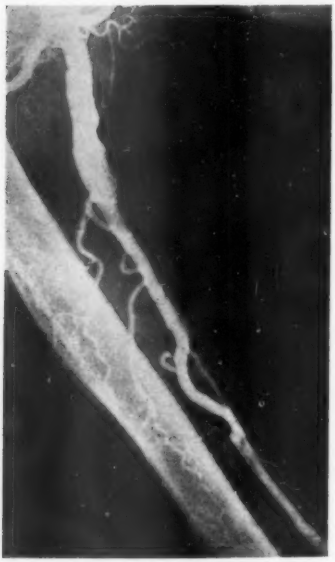
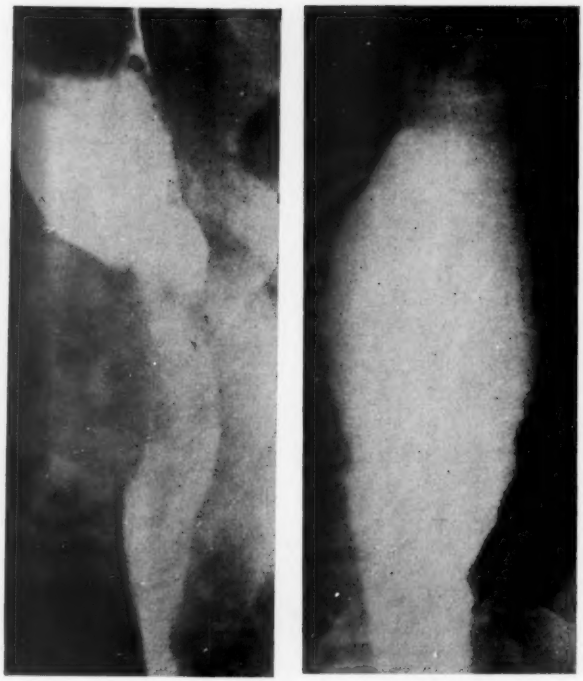


FIG. 5.—Aneurysm of brachial artery.

FIG. 6.—Giant aneurysm of ascending aorta.



A B

FIG. 7A and B.—Thoracic aneurysm causing dysphagia. (A) Barium swallow showing obstruction; (B) Retrograde percutaneous femoral catheterization showing aneurysm.

TABLE I.—INJECTION BY NEEDLE

Artery punctured	Ease of puncture	Volume of contrast in ml.	Strength of Diodone per cent
Abdominal aorta ..	+	20 to 30	70
Femoral artery ..	+	20 to 30	35 or 42
Carotid artery ..	++ to +++	10	35 or 42
Subclavian artery ..	++ to +++	20	35 or 42
Brachial artery ..	++ to +++	15	35
Vertebral artery ..	+++	8	35
Popliteal artery ..	+++	15	35

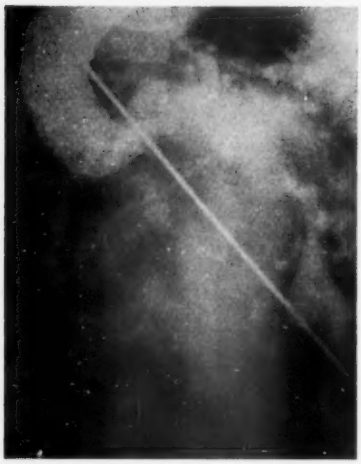
+ = Easy. ++ = Requires experience. +++ = Difficult.

TABLE II.—INJECTION BY CATHETER

Artery punctured	Ease of puncture	Catheter tip sited	Volume of contrast in ml.	Strength of Diodone per cent
Femoral	++	(*a*) Iliac artery	20	50
		(*b*) Abdominal aorta	20 to 30	70
		(*c*) Descending thoracic aorta	20 to 30	50 to 70
Carotid	++ to +++	(*a*) Ascending aorta	30 to 50	50 to 70
		(*b*) Carotid artery	10	35 or 42
Brachial	++ to +++	(*a*) Subclavian	20	35 or 42
		(*b*) Vertebral	8	35

The lesions of the major vessels will be discussed under five main pathological headings:

1. Congenital and developmental anomalies.
2. Obstructive lesions—thromboses; stenoses; embolisms.
3. Aneurysms.
4. Arterio-venous fistulas.
5. Angioma and miscellaneous lesions.



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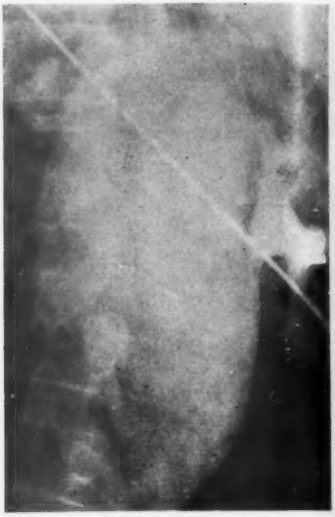


B

C

FIG. 8A and B.—Abdominal coarctation with post-stenotic aneurysm (*see also* Fig. 15).

FIG. 8C.—Post-mortem specimen. Aorta laid open to show the coarctation at the level of the renal arteries. The superior mesenteric artery and cœliac axis are seen to arise just above the coarctation.

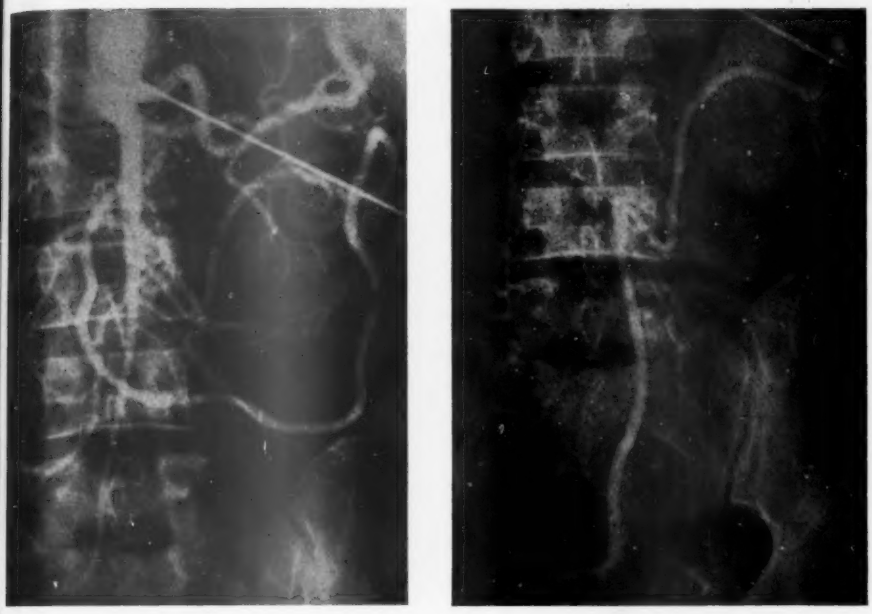
We shall deal separately with first the thoracic aorta and its major branches, and secondly with the abdominal aorta and its major branches.

THE THORACIC AORTA AND ITS BRANCHES

Lesions distal to the thoracic inlet are most easily investigated by simple needle puncture of the carotid, subclavian or brachial arteries as described above. Intrathoracic lesions present a more difficult problem. The technique we have used in these cases has, as already noted, consisted of percutaneous puncture and catheterization from the carotid artery in the neck. The lesions encountered in the region under consideration, classifying them in accordance with the scheme set out above, are as follows:

(1) Congenital lesions: (*a*) coarctation of the aorta; (*b*) developmental anomalies of the great vessels; (*c*) patent ductus.
(2) Obstructive lesions: thromboses of major branches of the aorta and of the carotid and brachial arteries.
(3) Aneurysms involving the thoracic aorta and its major branches.
(4) Arterio-venous fistulas.
(5) Other lesions.

The congenital lesions.—We have now investigated 8 cases of *coarctation of the aorta* by our new technique, and have obtained satisfactory pictures in all. Fig. 1 is an example.



A B

FIG. 9A and B.—Aortic thrombosis, showing filling of inferior mesenteric artery from hypertrophied middle colic and left colic arteries.

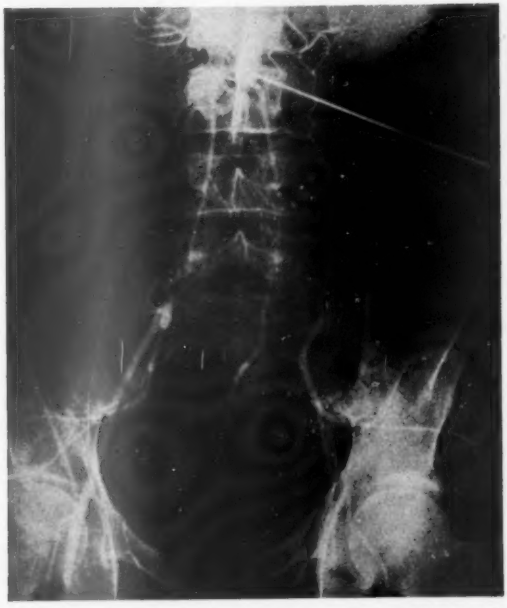
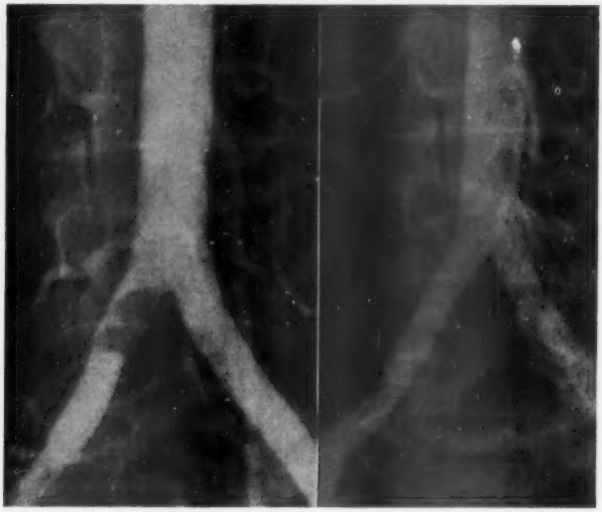


FIG. 10.—Aortic thrombosis, showing upper and lower limits of block.



A B

FIG. 11A and B.—Iliac occlusion, pre- and post-operative films.

FIG. 11C.—"Arteriolith" removed at operation.

FIG. 11D.—Radiograph of arteriolith showing extensive calcification.

FIG. 12.—Iliac thrombosis following pelvic irradiation.

A B

FIG. 13A. and B.—Abdominal aneurysm shown by femoral catheterization. (Serial films.)

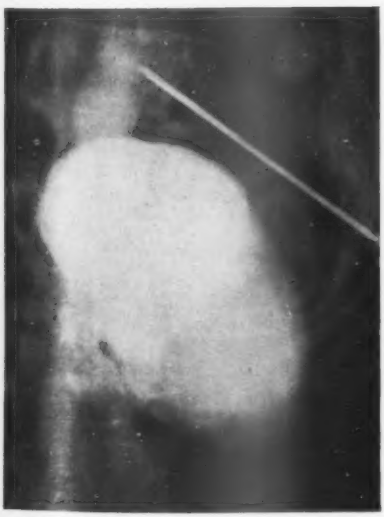


FIG. 14.—Mycotic aneurysm of the abdominal aorta at the origin of the inferior mesenteric artery.

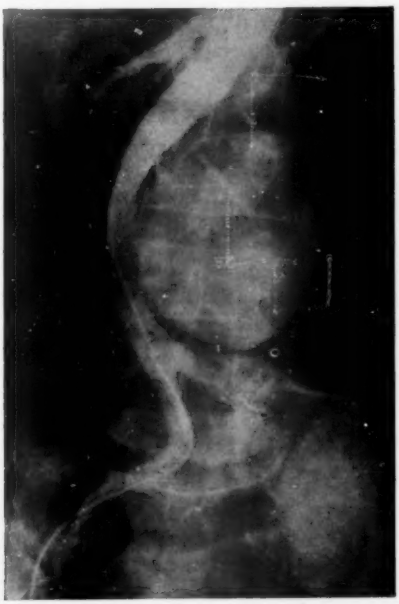
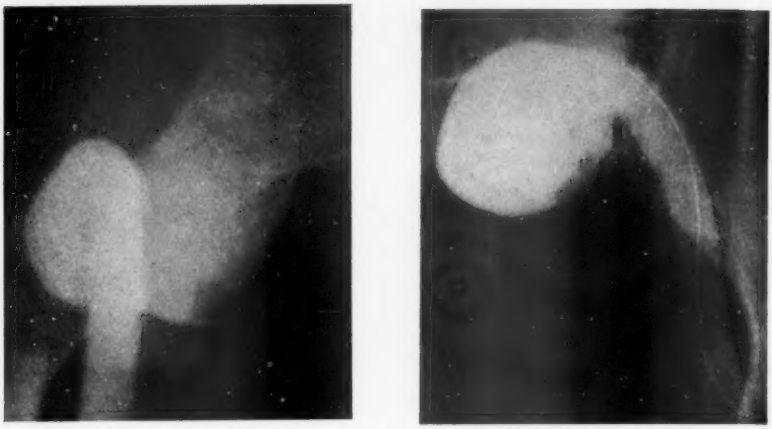


FIG. 16.—Saccular aortic aneurysm shown by femoral catheterization.



A B

FIG. 15A and B.—Femoral catheterization in case of giant abdominal aneurysm. On each side the catheter is blocked by kinking of the iliac artery, but the aneurysm extends down to the point of kinking. (Same case as Fig. 8.)

FIG. 17.—Arterio-venous fistula in the thigh. Note the retrograde venous filling.

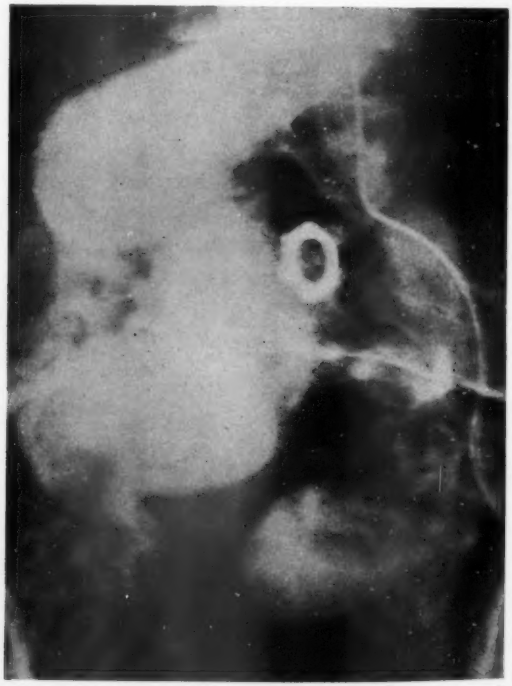


FIG. 18.—Huge arterio-venous fistula involving the internal iliac artery. Note the grenade cap and the enormous dilatation of the aorta, right common iliac and internal iliac arteries.

No examples have been encountered in our material of patent ductus investigated by thoracic aortography, but many cases have been so investigated and the lesion well shown by Jonsson and his colleagues in Stockholm using operative exposure of the radial artery and a catheter introduced from that point.

Amongst anomalies of the great vessels one case of dysphagia lusoria has been investigated and an anomalous right subclavian artery demonstrated.

Obstructive lesions of the great vessels.—These do not appear to have been previously demonstrated as occurring in the main branches of the aorta in the thorax, and I would therefore like to place on record 2 cases encountered in our material. The first was a patient of Dr. Denis Brinton's, presenting with symptoms of a left-sided cerebral lesion, possibly a tumour. Left carotid arteriography was attempted but we were quite unable to enter or even to palpate the vessel. At this stage we suspected a carotid thrombosis at an unusually low level in the common carotid artery. The opposite carotid artery was easily palpable. As there seemed no other method of filling the carotid artery Dr. Brinton agreed to my performing thoracic aortography by catheterization from the other carotid artery. This was done and an intrathoracic thrombosis of the left common carotid artery was demonstrated (Fig. 2).

Thrombosis of the internal carotid artery in the neck is a well-recognized syndrome but this is the first case we have encountered of an intrathoracic thrombosis of the carotid artery. It is, as far as we are aware, the first case which has been demonstrated by angiography in a living subject.

The next case is one of intrathoracic thrombosis of the subclavian artery and stenosis of the origin of the left common carotid (Fig. 3A and B). This patient had an aneurysm of the innominate artery of syphilitic ætiology. There were no symptoms referable to the left arm or brain but blood pressure readings were high in the right arm and not obtainable in the left.

We may anticipate from these 2 cases that intrathoracic thromboses of the great vessels will be demonstrated in increasing numbers in future years.

Both these cases were of syphilitic origin and associated with specific aortitis. Outside the thorax thrombosis of the carotid arteries is more common. My personal material now includes some 30 cases of thrombosis of the internal carotid artery, 2 cases of thrombosis of the common carotid artery, and 1 case of thrombosis of the external carotid artery. In most cases atheroma was the ætiological factor.

These were amongst over 2,000 carotid arteriograms performed in the last eight years. The appearances of thrombosis of the carotid artery in the neck are well known.

We have also seen 2 remarkable cases of localized stenosis of the internal carotid artery; in both cases the stenoses were due to localized atheromatous plaques at the usual site for carotid thrombosis, i.e. just above the common carotid bifurcation, and in both cases neurological signs were already present. These cases appear to represent pre-occlusion stages in carotid thrombosis.

One of these, where the symptoms were relatively mild, was successfully operated on, the atheromatous plaque excised and an end-to-end anastomosis of the carotid artery performed, with a good clinical result. (Eastcott, Pickering and Rob, 1954.) The other case was that of an elderly man in poor general condition, who had already developed a profound hemiplegia. Operation was not considered in his case.

We have one case of thrombosis of the subclavian artery in the neck amongst our material, and we have encountered several cases of thrombosis of the brachial artery in all of which the ætiology was traumatic, being due to pressure upon the artery from the prolonged use of a crutch (Fig. 4).

Arterial damage from this cause is not infrequent, and a paper by Professor C. Rob and Mr. A. Standeven on the subject will shortly be published. Apart from thrombosis of the brachial artery damage to the artery from crutch pressure can give rise to aneurysm (Fig. 5).

We have investigated a number of thoracic *aneurysms* by thoracic aortography with satisfactory diagnostic results. Our experiences, however, have shown that giant aneurysms of the aorta should be investigated with extreme caution. The only fatalities in our very large series of angiograms have, in fact, occurred in 2 cases of giant aortic aneurysm presenting through the thoracic wall or in the root of the neck (Fig. 6).

Both these cases died within twenty-four hours of a thoracic aortogram. In 1 case death was considered to be due to the anæsthetic and was ascribed by the Coroner to so-called "vagal inhibition". This patient collapsed and died immediately his endotracheal tube was removed. In the other case, no cause for death could be found. The patient failed to come round from the anæsthetic and died eight hours after the investigation. Both these patients had, at autopsy, gross coronary artery stenosis and were clearly very poor anæsthetic and operative risks. Investigation in their cases was only considered because of the obviously fatal nature of their lesions, i.e. giant aneurysms of the ascending aorta

presenting through the thoracic wall and rapidly enlarging. The only possible hope for both these patients was a successful operative removal. Isolated operative successes in this type of case have, in fact, already been recorded in the human, following upon successful animal experimentation. Despite these two fatal cases of giant aneurysm we feel that smaller and less spectacular aneurysms can be safely investigated. A number of such thoracic aneurysms have been successfully demonstrated by percutaneous catheterization (Sutton, 1955–56).

An aneurysm of the descending thoracic aorta can best be investigated by the simpler technique of percutaneous catheterization from below, the catheter being inserted from the femoral artery.

The next case presented clinically with dysphagia. The diagnosis when the patient was sent for examination was carcinoma of the œsophagus, because of a history of an obstructive lesion which might reasonably have been attributed to a neoplasm. The barium examination was performed by Dr. D. A. Symers. The possibility of an aneurysm causing pressure on the œsophagus was suggested, and thoracic aortography by catheterization from below was performed. This fully proved the diagnosis (Fig. 7A and B).

Another remarkable instance was that of a young man with a giant thoraco-abdominal aneurysm presenting in the loin (Rob, 1955); (*see also* Sutton, 1955–6). It was probably the first case in which a successful aortic graft was inserted in this country for aortic aneurysm above the renal arteries. There are now a number of cases on record where long-term successes have been obtained with this type and even with aneurysm of the aortic arch.

Aneurysm of the innominate artery is rare, but a case has already been illustrated associated with a subclavian thrombosis (Fig. 3).

Aneurysm of the subclavian, cervical carotid or brachial arteries is also rather rare. We have seen 2 examples of carotid aneurysm in the neck and have encountered 2 examples of brachial aneurysm and 1 of subclavian aneurysm.

We have encountered no examples of *arterio-venous fistula* and *angiomatous malformation* involving the thoracic aorta and its major branches although they have been encountered more peripherally. A case of angioma of the hand has been investigated by subclavian angiography (Sutton, 1955).

A second similar case was investigated by brachial arteriography. Angiomatous malformation is very common intracranially and about 100 such cases have been seen in my cerebral arteriogram material. 4 cases of extracranial angioma in the distribution of the external carotid artery have also been investigated by carotid angiography. Arterio-venous fistula has proved less common. 6 cases have been encountered in the cavernous sinus, and 2 in the upper limb.

The Abdominal Aorta and Its Main Branches

The techniques used for these arteries have consisted of: (1) Simple needle puncture of the lumbar aorta or of the femoral artery. (2) Percutaneous catheterization of the aorta or iliac arteries from the femoral artery.

The pathological lesions:

(1) Congenital and developmental: (*a*) Aberrant vessels; (*b*) abdominal coarctation.
(2) Obstructive lesions: Thromboses; stenoses; emboli.
(3) Aneurysms.
(4) Arterio-venous fistulas.
(5) Angiomas and miscellaneous.

Congenital lesions: Such anomalies as aberrant and anomalous renal arteries are not uncommon and about twelve cases have been seen in our material. However, these hardly enter the scope of our present discussion, and will not be described in detail.

One most unusual lesion encountered in a case of unilateral arterial insufficiency was a peculiar straight narrow and hypoplastic iliac artery, connecting the aorta and femoral artery on one side. In the absence of any satisfactory explanation for this odd appearance, we assumed it to be of congenital origin. The films have already been published by Professor Rob (Rob, 1955).

Another rare congenital lesion encountered was a case of abdominal coarctation of the aorta. This case presented as an abdominal aneurysm in a middle-aged woman. It was in fact a post-stenotic aneurysm, but its true nature was not discovered till autopsy (Fig. 8A, B, and C). This case will be described in more detail in connexion with aneurysms of the abdominal aorta.

Obstructive lesions in the abdominal aorta and its major branches are very common indeed. We have performed aortograms on a considerable number of cases in the last three years. These include 20 cases of thrombosis of the abdominal aorta, and some 60

cases of thrombosis of the iliac arteries. Even more common are thromboses of the femoral and more distal arteries. In the last six years I have in fact performed peripheral arteriograms on some 400 such cases of femoral thrombosis.

With aortic thrombosis the investigation is performed by lumbar aortography. The thrombosis does not extend above the renal arteries although it may extend to the point of origin of the renals. In at least one of our cases a renal artery has been involved in the occlusive process.

The inferior mesenteric artery is usually involved unless the thrombosis is restricted to the aortic bifurcation and has not yet extended up the aorta. Despite this occlusion of the inferior mesenteric artery the bowel it supplies still survives because of adequate anastomoses existing from the hæmorrhoidal arteries and from the middle colic branch of the superior mesenteric artery. This artery often hypertrophies to a remarkable size giving rise to a rather unusual appearance. Several articles have been published with illustrations of the condition of aortic thrombosis in which this unusual vessel is shown, but its significance has not been understood or has been mis-interpreted (Fig. 9A and B).

With aortic thrombosis it is of course vital to show by serial films the lower limits of the occlusion, the major anastomotic vessels, and the state of the distal vessels because surgical cure may be attempted. Much of this information can be derived from a careful study of serial aortogram films (Fig. 10).

Nearly all our 20 cases of aortic thrombosis have been seen in the last three years so that the condition must be much commoner than was previously supposed even allowing for the fact that at a special centre one will see greater numbers of these cases. The majority of cases of aortic occlusion were of course secondary to atheroma of the abdominal aorta or its bifurcation. Atheroma is also the commonest cause of occlusion of the iliac arteries.

One most unusual case was that of a young man with an iliac occlusion which on arteriography showed a clear-cut filling defect in otherwise healthy arteries (Fig. 11A and B). At operation what appeared to be a stony hard, calcified, thrombus was found adherent to the arterial wall and was removed by Professor Rob with excellent results (Fig. 11C). The specimen was later X-rayed and appears to be well described as an arteriolith (Fig. 11D). We have not encountered any similar case described in the literature, and it is an extremely puzzling case. Another most unusual case was an iliac thrombosis following pelvic irradiation for malignant disease (Fig. 12).

Aneurysms of the abdominal aorta are, like thromboses, commoner than used to be realized. We have performed aortograms on some 50 cases of abdominal aneurysm in the last three years. Most of these cases have been in men and the main ætiological factor is atheromatous disease of the aorta. Most cases of aortic abdominal aneurysm are best investigated by lumbar aortography. Upward extension of these atheromatous aneurysms, like upward extension of an aortic thrombosis, seems to be limited by the renal arteries and the atheromatous aneurysm hardly ever extends above them. Thus it is usually quite safe to puncture the aorta in the region of D.12/L.1 and to expect the needle to be above the level of the aneurysm. In an occasional case only, has this not turned out to be a practical procedure. In one such isolated case, although the aorta above the renals was not affected, it had been kinked and pushed aside by the enormous size of a sub-renal aneurysm (Fig. 8A). This is the case found at autopsy to be due to post-stenotic aneurysm in a case of abdominal coarctation at the level of the renal arteries (Fig. 8C). In this case we might easily have entered the aneurysm itself, but fortunately did not. Whilst upward extension of these aneurysms is as a rule limited by the renal arteries, downward extension may occur into one or both iliac arteries, although it is unusual for the aneurysm to extend beyond the bifurcation of the common iliac. The lumen of the aneurysm is often surprisingly small relative to the clinical mass, and in these cases there may be seen a large soft tissue shadow surrounding the lumen as shown at aortography. This is presumably due to clot. Sometimes the clot in the aneurysm shows as half shadow.

In most of these aneurysms of the lower abdominal aorta the inferior mesenteric artery is involved and may be occluded as it is in aortic thrombosis. For the reasons already stated no clinical effects of this inferior mesenteric obstruction are usually found.

Many of these cases have been successfully operated on and grafted (Fig. 13 A and B show a case investigated by femoral catheterization).

Though atheroma is the commonest cause of aneurysm of the abdominal aorta cases due to other ætiology are encountered. We have seen several cases of mycotic aneurysm in our material. In one case an aneurysm was demonstrated which at operation proved to be due to involvement of the aorta by a tuberculous gland. The lesion was successfully removed by Professor Rob and Mr. Eastcott and replaced by a plastic graft with good results. The films have already been published by my colleagues (Rob and Eastcott, 1955).

Another case of mycotic aneurysm was a patient of Mr. Dickson Wright's, who presented with irregular pyrexia and a pulsating mass in the abdomen. Aortography showed a very localized lesion which appeared to be arising about the region of the inferior mesenteric artery (Fig. 14).

Judging from the aortograms the lesion might have been amenable to surgery and operation was proceeded with. Unfortunately the aortogram proved rather deceptive because it did not demonstrate that the aneurysm was bound by adhesions to adjacent tissues and that it could not be removed without doing severe damage to vital structures. The attempt at removal had therefore to be abandoned, and several weeks later the patient died from rupture of the aneurysm.

Most abdominal aneurysms are investigated by lumbar aortography with adequate results. However, when the aneurysm is unusually large the contrast medium may become so dilute within it that its lower margins cannot be clearly defined. In some of these cases it may be necessary to resort to additional procedures in order to define the whole of the anatomical lesion. I have already shown an unusual giant abdominal aortic aneurysm, due to abdominal coarctation. This was first examined by lumbar aortography and the upper margins and certain anatomical details were well shown, but the lower limits were not defined (Fig. 8). It was therefore decided to perform a retrograde femoral catheterization in order to complete the anatomical picture (Fig. 15A). It was necessary in fact to repeat the femoral catheterization on the opposite side before the full anatomical picture could be built up (Fig. 15B).

In this case three arteriographic procedures were performed and a team of radiologists and radiographers were occupied for several hours before the films defining the whole anatomy of the aneurysm could be obtained. We have several similar examples in our material. In some cases technical difficulties may defeat all our attempts to obtain a complete picture. Thus, elderly people often have markedly kinked iliac vessels which will foil attempts at retrograde catheterization because the catheter cannot be passed through the kinked segment of the artery, exactly as in the case just shown.

Another type of case which presents considerable technical difficulty is that of saccular aneurysm with a relatively small neck. In one case several injections had to be made and adequate filling of the aneurysm was only obtained when the catheter tip was sited at a critical point opposite the neck of the aneurysm (Fig. 16).

It is clear from what I have been saying that the delineation of an abdominal aneurysm is not always a matter of simple routine investigation and that considerable patience and the ability to use several alternative methods are required by the radiologist who is investigating them.

Aneurysms of the iliac, femoral and popliteal arteries have been less frequent in our material, though we have seen a fair number of cases, the popliteal artery being the most frequently involved.

Arterio-venous fistulas may present a difficult technical problem to the radiologist. The important point to remember is that the shunt of blood through the fistula is usually so rapid that contrast media injected in normal quantities and concentrations and at normal pressures may be swept through too rapidly to be clearly shown on X-ray films. It is therefore necessary to inject larger quantities and concentrations of the drugs at increased pressures to obtain adequate films. Further, the serial films must be taken very rapidly as most of the contrast will be in the venous system within a second of the termination of injection. Figs. 17 and 18 show two examples of arterio-venous fistula. The first was in the thigh (Fig. 17).

Normally we obtain good visualization of the femoral artery with 20 c.c. of 35% Diodone; here 30 c.c. of 50% Diodone were used and this was injected at an increased pressure. The visualization of the vessels though adequate for diagnostic purposes is less dense than usual. An interesting point is the retrograde filling of the femoral vein below the point of the fistula owing to the venous pressure being locally increased at the fistula. The anatomy of the vessels however is in this case fairly easy to identify. This is not always so, and arterio-venous fistulas can produce very difficult problems of interpretation.

Fig. 18 shows a giant arterio-venous fistula involving the iliac vessels. This followed on a war wound from a hand grenade. The pictures were obtained by retrograde percutaneous femoral catheterization from the normal side. This investigation involved a 1½-hour session in the X-ray Department. Eventually diagnostic pictures were obtained by siting the catheter tip at the aortic bifurcation and injecting 40 c.c. of 70% Diaginol by a pressure machine and using a pressure of 80 lb. per square inch. Rapid serial films were taken mechanically, but only the first three pictures taken within 3 seconds were diagnostically valuable (Fig. 18). Having after so much time and trouble obtained pictures we found they were not at all easy to interpret. Prior to the operation we felt that a large straight vessel passing downwards was possibly a vein. However, this was not the case,

and at operation the aortogram findings did prove of assistance when they could be correlated directly with what the surgeon was exposing. Without an arteriogram it must have proved extremely difficult to assess the nature and significance of the distorted and enlarged vessels encountered. The actual anatomy is as follows: the large vessel passing downwards is an enlarged external iliac artery and the actual fistula is related to the internal iliac artery. The enlargement of the external iliac is explained by the fact that it arises above the level of the fistula. Even when all this was realized and the site of the fistula more or less accurately localized it proved a most difficult lesion to deal with, and necessitated a long and serious operation.

[This paper was illustrated by some 70 slides. Limitation of space allows only a representative selection of these to be reproduced.]

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Professor C. G. Rob (Professor of Surgery, St. Mary's Hospital, London):

Treatment and Results

I will discuss only those surgical procedures which aim at restoring the blood flow through an occluded artery or reconstructing the vessel after removal of an aneurysm. I shall not discuss sympathectomy, minor surgical procedures or conservative treatment beyond stressing that, in my opinion, direct surgical operations are only justified in a small minority of patients with obliterative vascular disease and that the treatment of choice for the majority is conservative with long-term anticoagulants. In the case of aneurysms the position is different; here operation is justified if they threaten life or cause severe symptoms.

An artery may be repaired by a direct anastomosis, the operation of thromboendarterectomy, the insertion of an autogenous or homologous blood vessel graft or with an implant of plastic material. Other procedures such as endoaneurysmorrhaphy and the insertion of heterologous blood vessel transplants are rarely employed today. We have experience of ninety-nine homologous arterial transplants, twenty-five autogenous vein grafts, nineteen reconstructions with a prosthesis of plastic cloth, twenty-three reconstructions with a tube of polyvinyl alcohol sponge, thirteen thromboendarterectomies and at least twenty-five direct arterial repairs. It is upon this that our conclusions have been based.

Today arterial banks are rapidly becoming obsolete, only seven years after the first clinical use of preserved arterial segments by Gross and his colleagues (1949) in Boston. In fact, we prefer a plastic prosthesis for arteries of the size of the human external iliac or larger, and consider that the results are as good with less risk to the patient and considerably less trouble for the surgeon and his team. For the reconstruction of peripheral arteries we still prefer a homologous arterial transplant but feel that an autogenous vein graft in experienced hands may give better long-term results, and we have great hopes that a satisfactory plastic prosthesis will soon be available for use in these smaller vessels.

A direct anastomosis is the best method of repairing a blood vessel and it is surprising how often it is possible to close the gap by this means. This is particularly so in patients with atherosclerosis because the artery in such patients is often lengthened and tortuous; this, after mobilization, allows the surgeon to close a fairly long defect by direct suture.

Thromboendarterectomy gives very good results in the right patient but the disease should be well localized in a large vessel. Our results with this operation in a highly selected group of cases have been good, 12 out of 13 patients having patent vessels today.

Autogenous vein grafts may do well but in our experience many patients with obliterative arterial disease have abnormal veins as well, and this is one of the reasons why the results are disappointing in these patients. On the other hand, we have inserted 99 homologous arterial transplants (frozen and freeze dried) with 7 deaths and 14 thromboses in hospital. Of the remaining 78 patients at least 21 have thrombosed since discharge and 17 of these patients suffered from some form of obliterative arterial disease.

In the case of plastic prostheses we have inserted forty-two mostly into large vessels, only two have thrombosed but 10 are dead, one from failure of the prosthesis due to infection and the majority of the others from coronary artery disease. A variety of plastic prostheses have been used for the reconstruction of arteries, notably the plastic cloths of which Vinyon

N cloth was the first to be used by Voorhees, Jaretzki and Blakemore (1952). More recently a number of other plastic cloths have been used, notably nylon, Orlon, terylene and a multi-layered fabric composed of nylon and polythene (Shumacker and King, 1954). Of these it appears that Orlon and terylene are the best. The use of Orlon was pioneered by Hufnagel. In 1955 he published the results of his experimental and clinical work. He had inserted an Orlon prosthesis into 15 patients over a period of sixteen months with good results. In this country Kinmonth, Taylor and Lee (1955) have also found it satisfactory. We have used a prosthesis of plastic cloth on nineteen occasions in patients. In spite of the successes obtained by Hufnagel, ourselves and others with the plastic cloths, they are not ideal and polyvinyl alcohol sponge (Prosthex) prepared in the manner recommended by Shumway, Gliedman and Lewis (1955) and Owen (1955) is, I think, better and has proved satisfactory in 22 of our patients, but the long-term results here and with the plastic cloths are not yet known.

In my view, the results of this type of surgery depend more upon the reason for inserting the transplant than upon the type of repair or material used. Table I gives our results in 85 patients with occlusive arterial disease and Table II in 55 patients with an aneurysm, and it will be seen that, apart from the mortality which is much higher in the patients with aortic aneurysms due to coronary occlusion after these major procedures and the number of emergency operations upon leaking aneurysms, the results are better in those patients whose arterial disease has taken the form of dilatation rather than obliteration.

TABLE I.—85 ARTERIAL RECONSTRUCTIONS IN PATIENTS WITH OCCLUSIVE ARTERIAL DISEASE

Vessel	Number of reconstructions	Thrombosed in hospital	Thrombosed later	Patent today
Aorta and iliacs ..	28 (2 died in hospital)	1	1	24
Femoral	37	11	7 (+ 1 dead since discharge)	18
Popliteal	15	1	5	9
Others	5	2	2	1

3 have thrombosed another artery since operation.

TABLE II.—55 RECONSTRUCTIONS IN PATIENTS WITH ARTERIAL ANEURYSMS

Vessel	Number of aneurysms	Thrombosed in hospital	Thrombosed later	Patent today
Aorta and iliacs ..	36 (9 died)	0	0	27
Femoral	8	2	0	6
Popliteal	8	1	1 died 6 months later	6
Others	3	2	0	1

Another very important factor is the size of the vessel, and in general terms the larger it is the better the results. An apparent exception to this is provided by the femoral and popliteal arteries, the results being much better in the slightly smaller popliteal artery particularly of patients with occlusive arterial disease. In my view, this is due to the fact that an occlusion of the superficial femoral artery, particularly if it is well localized, may give rise to relatively mild symptoms and it is often only in those with marked atherosclerosis that a surgical operation is justified. On the other hand, occlusion of the popliteal artery may produce crippling symptoms in a patient with an apparently normal vascular tree and under such circumstances a reconstruction operation is more likely to succeed.

In conclusion, we have performed more than 180 direct surgical operations upon the arteries of patients and the longer term results have improved with better selection. In occlusive disease this must be strict, but in patients with aneurysms, injuries, etc., we are advising operation more and more frequently.

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Section of Pathology

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[*March* 20, 1956]

Anaphylactic Reactions of the Mesenteric Blood Vessels of the Rabbit

A Film[1] by J. HUGUES, M.D., and J. LECOMTE, M.D.
(*presented by J. Lecomte, M.D., University of Liége, Belgium*)

THE morphological modifications of sensitized vessels submitted to an allergic reaction have already been observed *in vivo* by Gerlach who, in 1923, used for this purpose the mesenteric vessels of frog. Abell and Schenck (1938), Ebert and co-workers (1949, 1951) performed similar experiments in rabbits, making use of Clark's ear chamber technique. Burriage and Irwin described, in 1953, the anaphylactic reactions of pleural capillaries.

We have studied the changes occurring in the mesenteric vessels of the rabbit when they have been submitted to the specific antigen. Such anatomical preparations are very easily studied (Hugues, 1953): the blood vessels are clearly seen and the analysis of early allergic vascular changes is very simple.

[The film demonstrated a few of these experiments.]

We have used rabbits (average weight 2 kg.), actively sensitized by ovalbumin three weeks prior to the experiments. Under chloralose anæsthesia, the abdominal wall is cut along the mid-line and the meso-appendix is fixed to the muscles. The intestine is carefully pulled outside of the abdominal cavity, without any other manipulation.

In normal rabbits, the contact of mesenteric vessels with ovalbumin does not elicit any visible change.

In ovalbumin-sensitized rabbits, successive vascular alterations are detected shortly after the contact with the antigen. During the first five minutes, the *venous* walls show important changes. Platelets and leucocytes adhere to the endothelium and form a layer which markedly reduces the lumen of the veins. No vasomotor changes are observed.

After eight minutes, emboli are seen in the venous flow. Their length ranges between 50 and 100μ. They are formed at the venous junctions where these accretions become detached from the endothelium. Some of these emboli are suddenly stopped by the platelets adhering to the walls.

After fifteen minutes, venous walls rupture at some points, and red cells invade the neighbouring tissues. The vascular ruptures are sometimes so prominent that purpuric spots are visible with the naked eye.

After thirty minutes, venous circulation is stopped. Arterioles are normal. There is no important leucocytic infiltration.

The general anaphylactic shock induced by intravenous injection of albumin sometimes results in death of the sensitized rabbit.

Even in such cases, no modification occurs in the mesenteric circulation.

[1](For technical details, *see* Lecomte, J., and Hugues, J., 1956.)

Local application of thrombin induces a progressive adherence of platelets and leucocytes to the venous and arterial walls. This layer grows rapidly and finally circulation stops completely. The accretions are sometimes released from the endothelium, producing emboli in the venous flow. At the end of this process, some wall ruptures become visible: they lead to the appearance of purpura, both venous and arterial.

Allergic reactions which occur in the mesentery induce changes in the histamine content of this membrane (Lecomte, 1956). This content drops from 3·8 μg/g. to 0·2 μg/g. during the first ten minutes. Later, however, after the reaction has fully developed, the histamine content increases up to 12 to 20 μg/g. This increase is due to the agglutination of the platelets.

Local application of histamine liberators such as 48/80 or 1935 L in a 0·1% solution induces an important decrease of the histamine content of the membrane (Lecomte, 1956). This total histamine depletion does not produce any anatomical change nor does it modify the early allergic modifications of the blood vessels.

Local application of 0·1% histamine solution is not followed by any visible vascular changes. The same negative result is obtained after intravenous injection of a lethal dose of histamine.

Intravenous injection of promethazine prior to the local application of the antigen does not at all modify the allergic anatomical reactions of the mesenteric vessels.

Histamine does not play any important role in the mechanism of platelet agglutination or vascular rupture.

The same negative results are obtained when 5-hydroxytryptamine is used instead of histamine.

Crude trypsin (0·1%) has also been applied on the mesentery. After fifteen minutes, venous walls are ruptured, and red cells invade the neighbouring tissues. Finally marked purpura is produced but agglutination of the platelets or their adherence to the vascular walls is never observed.

A fundamental difference seems to separate anaphylactic damage and local disturbances induced by proteolytic enzymes.

Injections of cortisone (10 mg.) and corticotrophin (12·5 mg.), repeated five times during the three days before antigen applications, reduce the degree of subsequent vascular damage.

Calcium gluconate (1·6 grams) and sodium salicylate (150 mg.) have a similar inhibiting effect when they are injected intravenously just before the local application of ovalbumin. This anti-allergic property of sodium salicylate is not due to activation of the hypophyso-adrenocortical system (Van Cauwenberge and Lecomte, 1955). Heparin in large doses (50 mg.) completely inhibits the anaphylactic reactions; in the present state of our knowledge, this substance seems to be the only agent which is capable of completely inhibiting morphological vascular reactions of allergic origin (Lecomte and Hugues, 1954).

Our present concepts regarding the pathogenesis of these morphological vascular reactions may be summarized as follows: Antigen-antibody reactions occurring in the endothelial cells of vein walls rapidly induce some undetermined change in these cells, leading to the release of local thromboplastic substances. The latter are responsible for local blood clotting, with agglutination of platelets at their site, and subsequent formation of emboli. As the endothelial damage increases, venous walls are ruptured and hæmorrhages appear.

Even though histamine is released in this process, it does not play any role in the mechanism of these anatomical reactions.

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Serum Globulins as Mediators of Pathological Changes of Capillary Permeability

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FRESH guinea-pig serum and plasma contain the inactive precursor of a large-molecular permeability factor (PF), which increases the permeability of the skin capillaries in the guinea-pig. The PF is activable by dilution in 0·85% saline and substantial amounts are formed in dilutions of 1/200–1/400 within one hour at room temperature; we have called this permeability factor PF/Dil to distinguish it from PF/Age, a second permeability factor which matures within a few days in neat serum held at 2° C. PF/Age contributes less than 0·5% to the PF potency which can be elicited in guinea-pig serum.

In low dilutions of serum (up to 1/50) the activated PF/Dil is antagonized by a low potency inhibitor (IPF), which seems to be present as such in serum, but of which more is activated by dilution to about 1/10.

Like histamine and leukotaxine, PF/Dil increases the permeability of skin capillaries within 3 min., and the capillaries recover their normal low permeability within 20 min. PF/Dil is not antagonized by the antihistamine drug mepyramine maleate. It is antagonized moderately by pancreatic trypsin inhibitor and strongly by small doses of soya-bean trypsin inhibitor (SBTI).

PF/Dil seems to be identical with a powerful PF obtained by fractionating guinea-pig serum in aqueous ethyl-ether systems. The PF is an α_2-globulin, of which about 1 mg. can be obtained from 1 ml. of serum. It is as potent as histamine on a weight basis and more than 2,000 times as potent on a molar basis. There is no evidence that PF α_2-globulin acts by liberating histamine. Its action in guinea-pig skin is readily inhibited by SBTI, suggesting that it is a protease, though it seems to be distinct from serum fibrinolysin.

The low potency serum IPF seems to be identical with a slowly-acting IPF fraction which inhibits both PF/Dil and PF α_2-globulin. IPF is an α_1-globulin, the best preparations of which inhibit about 1/800th of their weight of PF α_2-globulin preparations after 30 min. at room temperature and about 1/30th of their weight after four days at 2°.

The above results have been described in detail elsewhere (*see* Miles *et al.*, 1955; Wilhelm, Miles and Mackay, 1955). Permeability factors were tested by intracutaneous injection into depilated guinea-pigs given intravenous pontamine blue (*see* Miles and Miles, 1952). Similar methods have been used to investigate rat and rabbit serum preparations, each tested in the homologous species of animal.

Fresh neat guinea-pig serum tested in guinea-pigs is inactive; the inactivity is a species phenomenon, because in rats or rabbits it induces large lesions. Neat rat serum, on the other hand, induces large lesions in rats as well as in guinea-pigs and rabbits. Neat rabbit serum also induces large lesions when tested in rabbits or in guinea-pigs and rats. This permeability factor in the fresh neat mammalian sera we call PF/Neat.

In addition to PF/Neat, rat serum, like guinea-pig serum, contains a PF/Dil activable by dilution in saline. It first appears in 1/5–1/15 dilutions when they are 13–14 min. old. With increasing age, PF/Dil activity moves to higher dilutions, but cannot be detected beyond four hours. Presumably the native inhibitor in rat serum acts more quickly than guinea-pig IPF, leading to the more rapid disappearance of PF/Dil. Although, like rat serum, fresh neat rabbit serum contains a PF/Neat, we have failed to activate a PF/Dil in it, possibly because it contains a strong serum IPF.

As in the guinea-pig, a high proportion of the PF activity of rat and rabbit sera is in the G2 fractions, which consist of α- and β-globulins. These globulins have not yet been analysed electrophoretically. Rat and rabbit IPF have not yet been isolated, but indirect evidence suggests that rat and rabbit sera contain inhibitors.

The relative potencies of histamine, and of guinea-pig, rat and rabbit G2, tested in the three species of animals, vary according to the test animal. In all three species, the guinea-pig fraction is the most potent G2, but each variety of G2 is relatively most potent when tested in the skin of its homologous species.

Both SBTI and the guinea-pig IPF fraction, G1S/P, inhibit rat and rabbit G2. The varying potencies of these G2 fractions in the three species suggested that interspecies tests may offer a chance to determine where these inhibitors act. If they act on the serum PF,

we could expect, for a constant dose of PF preparation, that the dose of inhibitor would be constant whatever the test animal, i.e. inhibition on a weight basis. If these inhibitors act on a tissue protease, the amount of inhibitor should vary according to the potency of the PF preparation in the different species, i.e. inhibition on a potency basis.

The results of SBTI inhibition tests of guinea-pig and of rat PF, in both guinea-pigs and rats, suggest that SBTI acts on a tissue protease. This is consistent with the rate of apparent inhibition of PF by SBTI *in vitro*; 2-min.-old mixtures of PF and SBTI are inactive on injection. On the other hand, isolated guinea-pig IPF acts slowly *in vitro*; 85% of PF is inhibited in 30 min. and more than 99% in four days. These results indicate a direct action of the IPF on the PF and inhibition should therefore be on a weight basis. However, the numerical results are more consistent with potency rather than weight. Inhibition by SBTI on an approximate potency basis is not therefore valid evidence that the inhibitor acts on a tissue constituent rather than on PF.

The title of my paper is misleading because we are still as ignorant about the role of these factors in anaphylaxis and inflammation as we are about proteases, leukotaxine and histamine. The guinea-pig plasma system of PF and IPF appears to be rather stable, because it is unaffected by active and passive anaphylaxis, by cortisone treatment or even by sublethal irradiation sickness. We have not yet investigated the system in inflammation, because we felt that it was more important to establish that the PF discovered in guinea-pig serum was a general property of other mammalian sera. We are satisfied that a PF–IPF system, of the same general nature as in the guinea-pig, occurs in the rat, rabbit and man.

Our interspecies tests of serum PFs and their inhibition emphasize the importance of testing these substances, where possible, in animals of the homologous species, and indicate that, whereas the PF–IPF systems of the rat and man generally resemble that of the guinea-pig, the system in rabbit plasma is substantially different.

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Section of Proctology

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[*February* 8, 1956]

The Significance of Bleeding as a Symptom in Diverticulitis

By ANTONY J. RUSHFORD, M.B., F.R.C.S.

THIS paper deals with an investigation into the significance of rectal bleeding in colonic diverticulitis.

Introduction.—To investigate the possibility of bleeding arising in a colonic diverticulum it is necessary to examine the anatomy and structure of the tissues. Careful dissections of colonic diverticula have shown sizable blood vessels in their close proximity and indeed it is through weak spots alongside these vessels that the original protrusions occur.

The pathological findings in diverticula which had caused rectal bleeding show various grades of inflammation or even hæmorrhagic necrosis. Bleeding may also come from granulation tissue. This occurs either in the walls of diverticula or in the bowel wall adjacent to the mouths of the diverticula. The latter condition is associated with secondary colitis which may alone also be responsible for hæmorrhage into the bowel. The passage of a concretion from a diverticulum may cause bleeding and such an observation has actually been made. The investigation of such cases must include barium enema, sigmoidoscopy and occult blood tests. The majority of writers on this subject stress the need to exclude benign or malignant growths before attributing such bleeding to diverticulitis. The most striking clinical picture which has recently come to the fore is that of massive hæmorrhage from a previously unsuspected diverticulitis.

A bibliography of papers dealing with bleeding in diverticulitis is appended.

Treatment.—Conservative treatment in rectal bleeding in diverticulitis is advised by most surgeons who have had to deal with this condition. Cases are quoted, however, where a resection became necessary to prevent the recurrence of severe bleeding, or to remove a diagnostically doubtful swelling in the colon. Together with the increasing field of colonic surgery, resection is being more frequently advised and resorted to in cases of rectal bleeding in the presence of colonic diverticulitis (McNealy, 1955; Welch *et al.*, 1953). This course must always be taken in cases where there is any suspicion of a neoplasm. However, a conservative regime has usually been successful in controlling rectal bleeding and though occasional recurrences have been seen, these were more the exception than the rule. The regime consisted usually of a low or non-residue diet, liquid paraffin by mouth and possibly rectal instillation of warm olive oil. Intestinal antiseptics and antibiotics have also found a place in the cases where diarrhœa predominated. The blood loss was corrected by transfusion and oral iron was given.

The present series.—The present series comprises 120 cases of colonic diverticulitis seen over a five-year period. All the cases were thoroughly investigated by barium enema or meal, and by the proctoscope and sigmoidoscope. In 33 (27·5%) of these, rectal bleeding had been a symptom. Of these 15 (45%) were men and 18 (55%) women. reflecting approximately the overall sex distribution of the disease. The age distribution shows a peak in the 6th decade, in which a third of the cases occurred. The sigmoid colon alone was affected in 9 cases (27%), the descending colon in 12 cases (36%), in 6 cases (18%) the transverse and descending colon were affected and in 4 cases (12%) the whole colon was involved (Table I). The remaining 2 cases were too recent for a proper follow-up and are

TABLE I.—DISTRIBUTION OF DIVERTICULITIS

Sigmoid only	9	Sigmoid, descending and transverse	6
Sigmoid and descending colon	12	Generalized diverticulitis	4

not included in Table I. Barium enema revealed spasm in 15 cases (45%). The colour of the blood passed varied from bright red to black; in 9 cases (27%) the colour was dark red or black. It is interesting to note that 7 (21%) of these were cases of diverticulitis of the colon proximal to the splenic flexure. The length of history of bleeding extended from a few days to several years (Table II). The cases were followed up for periods of six months to five years (Table III). There were 5 who had been followed up for over five years and had all remained trouble free. 4 deaths occurred in the series; 2 from carcinoma, 1 of which was of the bronchus, 1 due to colitis and the last due to a severe rectal hæmorrhage. Resection was carried out on one case where a doubtful colonic mass proved to be a diverticular granuloma. Removal of this segment of the bowel prevented any further recurrence of

TABLE II.—LENGTH OF HISTORY

Time	No. of cases
0–1 month	11
1–6 months	8
6 months–2 years	6
2 years and over	8

TABLE III.—LENGTH OF FOLLOW-UP

Time	No. of cases	Result	
		Relieved	Not relieved
5 years	5	5	—
4 years	5	4	1 + Colitis
3 years	8	6	2 + Carcinoma
2 years	4	3	1 + Hæmorrhage
1 year	3	3	
0–1 year	6	6	

rectal bleeding. In 28 (85%) cases all rectal bleeding ceased soon after conservative treatment had been started. A recurrence of rectal bleeding after the institution of treatment was only found in 2 cases (6%).

Discussion.—This review was undertaken to investigate the incidence and significance of rectal bleeding caused by diverticulitis. In searching the literature some 90 papers were read, and an average incidence of 17% was found after computing figures from 45 different series of cases, amounting to 6,000 patients.

There is no doubt that diverticulitis can be responsible for bleeding into the bowel. This varies with the size of the vessel involved and the site of the lesion. Dark blood or melæna may be produced by proximal colonic diverticulitis. Massive hæmorrhage from the rectum may occur in a previously unsuspected colonic diverticulitis. The diagnosis can be established directly, only by either seeing blood issuing from a diverticular orifice on sigmoidoscopy or after resection of the affected segment of the colon. However, it is also possible to arrive at the diagnosis by careful exclusion of other causes of rectal bleeding, especially carcinoma of the colon. This involves the examination of the rectum and colon, both clinically and radiologically, together with a careful follow-up system. If rectal bleeding persists after the institution of treatment the cause is most unlikely to be diverticulitis, and a laparotomy must be resorted to even if no positive findings of neoplasm are evident. Even if diverticulitis is found on X-ray, we are warned by Cuthbert Dukes (1939) that this may be coexistent with carcinoma of the colon in 12% of cases, while Lloyd-Davies (1953) found neoplasms in 6 out of 9 cases of diverticulitis with bleeding.

Summary.—This review has shown: (1) That rectal bleeding occurs in colonic diverticulitis at an average of 17% of cases. In my own series a higher figure of 27% was found.

(2) The quantity of bleeding varied from slight traces of blood to massive exsanguinating hæmorrhages requiring life-saving blood transfusion.

(3) Complete relief from bleeding can be obtained in a vast majority of cases (85% in my series) after the institution of a conservative regime. If, therefore, in spite of the above measures, rectal bleeding continues, other sources than diverticulitis must be sought.

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Retrograde Intussusception of the Colon

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FEW conditions have held the interest of surgeons over the course of the years in the way that intussusception has done. This is shown by the enormous literature on the subject. The main incidence of intussusception is, of course, in the first two years of life. A consecutive series of 400 cases from the London Hospital, reported by Perrin and Lindsay (1921), included 18 inpatients over the age of 14, so that only about 5% of all these intussusceptions were in adults. As this series covered the years 1903–20, there was an average during this period of one adult intussusception a year at the London Hospital. A similar incidence has been reported from the Massachusetts General Hospital (Lawrence and Ulfelder, 1952), which had 15 adult cases between 1937 and 1951. In series of cases in adults about 90% of the intussusceptions are due to tumours or other obvious cause (Brayton and Norris, 1954).

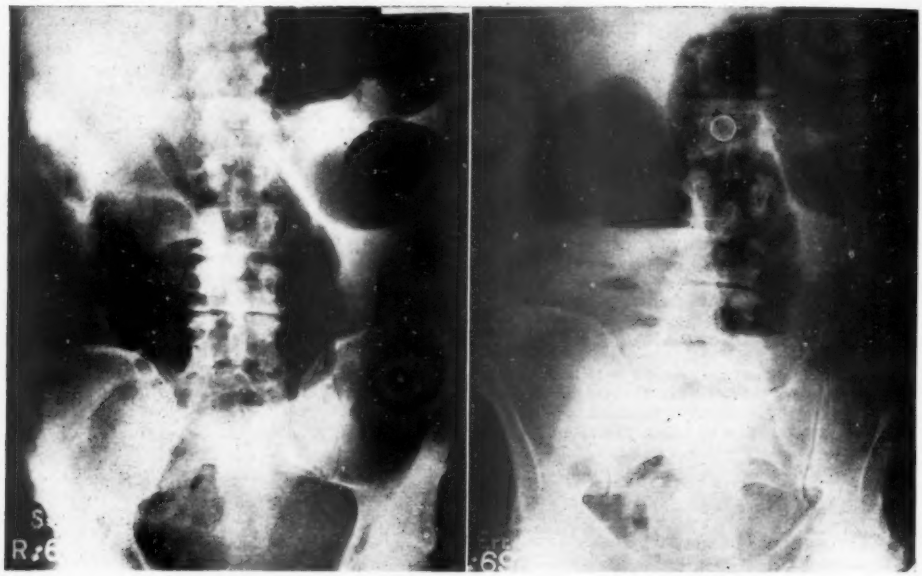
When intussusception occurs, it is usually downwards in the normal direction of peristalsis but occasionally it occurs in the reverse direction when the intussusception advances up the more proximal segment of the gut. In the London Hospital series of 400 cases there were 2 of retrograde intussusception, both enteric, giving an incidence of 0·5%. Akehurst (1955) has collected from the literature 103 cases of retrograde intussusception from different

parts of the alimentary tract and reported a further one. The case described below was a retrograde intussusception of the colon and there was no cause apparent for its production.

Case Report

History.—A man aged 63 was admitted as an emergency to Whittington Hospital, London, under the care of Mr. W. W. Davey who kindly allowed me to treat him. He had abdominal pain and absolute constipation of four days' duration. Previously regular daily bowel actions ceased abruptly with the onset of the pain, which was intermittent and colicky. There was no vomiting.

On examination.—He had a distended abdomen with high-pitched bowel sounds. His doctor had felt a mass in the left iliac fossa but this was not palpated in hospital. Radiographs supine and erect (Fig. 1) confirmed the diagnosis of intestinal obstruction and showed distension of the large bowel down to the lower descending colon. Laparotomy was therefore undertaken for intestinal obstruction, thought to be due to carcinoma of the pelvic colon.



A B

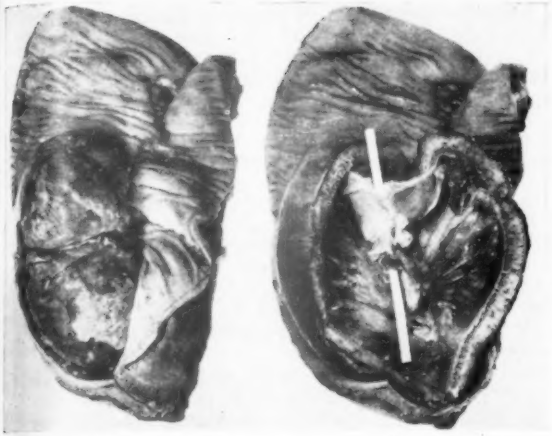
Fig. 1.—Straight radiographs of the abdomen—A, Supine; B, Erect—showing evidence of intestinal obstruction. The cause of the obstruction can be diagnosed from the supine film (*see* Fig. 3).

Operation.—The abdomen was opened through a lower right paramedian incision. The cæcum, transverse and descending colon were found to be greatly distended and a swelling was felt in the pelvis. This swelling was recognized on palpation as a retrograde intussusception of the pelvic colon because of its consistency, the characteristic feel of the apex and the sudden decrease in diameter at the neck, which was at the distal end. The colon was deflated with a needle attached to a sucker and the portion containing the intussusception mobilised, thus enabling it to be brought into the wound. Attempts to reduce the intussusception failed. Paul's operation was therefore done and the intussusception brought out through a small separate incision in the left iliac fossa. The main incision was closed, the intussusception excised and a Paul's tube tied into each loop.

Specimen.—It was expected that a neoplasm would be found in the intussusception but, as shown in Fig. 2, it proved to be idiopathic or primary. In the fresh state it was 12 cm. long, was much thickened and congested and of very doubtful viability at the apex. There was an acute ulcer in the colon adjacent to the apex of the intussusceptum, which was presumably caused by pressure of the intussusceptum. Histological examination (Dr. P. C. Meyer) showed acute inflammation, involving all coats of the bowel, in the region of the ulcer with destruction of the muscular coat. At the apex of the intussusceptum there was necrosis down to and including the circular muscle layer.

Recovery.—In due course the patient had the spur of the colostomy crushed and an extraperitoneal closure of the colostomy. Three months after his discharge from hospital sigmoidoscopy and barium enema showed no abnormality. Further questioning of the patient failed to discover any previous attacks of pain or bowel upset. He had had no previous operations nor any illnesses of note except malaria thirty-eight years previously.

Radiographic diagnosis.—When the radiographs were reviewed in the light of the operative findings, one of our radiologists noted that a soft tissue shadow corresponding to the intussusceptum could be seen on the supine film (Fig. 3). The convex surface of the apex was outlined by the shadow of the



A B

FIG. 2.—A and B, Idiopathic retrograde intussusception of the pelvic colon. The pressure ulcer produced by the intussusceptum is seen in the upper right hand corner. B, Intussusceptum opened with glass rod in the entering loop, which retracted on fixation into the middle of the specimen.

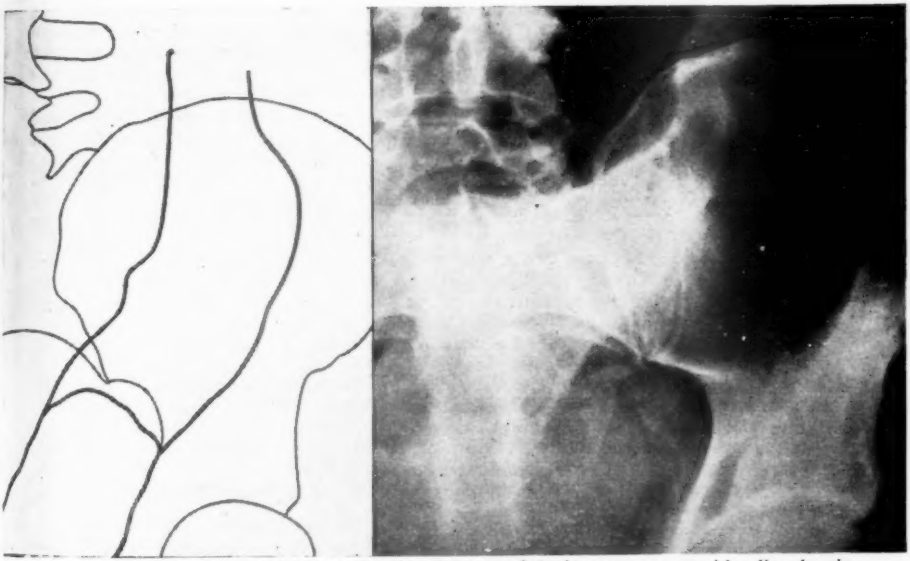


FIG. 3.—Part of the supine radiograph showing the apex of the intussusceptum with a line drawing to illustrate its position.

gas in the colon proximal to it. This appearance in reverse is, of course, characteristic of orthograde intussusception but it is very rare to see radiological evidence of retrograde intussusception.

DISCUSSION

Analysis of published cases.—There appear to be two main groups of retrograde intussusception of the colon—single and multiple. The case described above belongs to the single colo-colic group, of which Akehurst collected 11 cases and reported a 12th. In the multiple group two (rarely more) intussusceptions are present, one of which is retrograde and the other orthograde. An ileo-cæcal intussusception may be associated with a separate retrograde colo-colic, so that at operation the second intussusception might be missed. D'Arcy Power (1886) stated that "if laparotomy be performed for the relief of intussusception, it is as well before closing the abdomen to make quite sure that a second invagination is not present". Another combination is where an orthograde intussusception for some reason is halted and then reverses direction, the whole becoming a retrograde intussusception.

It is not surprising that this may be difficult to disentangle. A third combination in multiple intussusception is where orthograde and retrograde intussusceptions have met "head on" and one has telescoped the other. Multiple intussusception of the colon will not be discussed further except to note the rather curious fact that it seems considerably commoner than the single variety. There were 40 cases in Akehurst's series compared with 12 of the single group of retrograde colo-colic intussusception.

There are 2 other cases of single retrograde colo-colic intussusception in the literature—one reported by Teasdale (1953) in a woman of 51 due to a carcinomatous ulcer of the sigmoid colon and the second by Deterling *et al.* (1953) in a woman of 44, which was associated with a Miller-Abbott tube in the ascending colon. Including my own, the total number of cases reported would now appear to be 15, of whom 9 were in females, 4 in males and in 2 the sex was not stated. Of these 15 cases of single retrograde colo-colic intussusception, 9 have been idiopathic and 6 secondary. 4 in the idiopathic group of 9 were in children. 5 of the 6 secondary cases were due to neoplasm and the other case was associated with the Miller-Abbott tube in the ascending colon. Apart from this last case and another one in which details were not given, all the remaining 13 cases of retrograde intussusception originated in the descending or pelvic colon.

Ætiology.—Intussusception belongs to that group of physiological disorders of the alimentary tract about whose ætiology there is still so much to discover. Inflammatory swelling of lymphoid tissue, acting like a foreign body, is generally considered to be the cause of the common orthograde intussusception met in the first 2 years of life and a neoplasm the usual cause of intussusception in the adult. But this leaves us without an explanation of the idiopathic intussusception in the adult, which occurs occasionally in this country and more frequently in other countries. While I was on the staff of a Mission Hospital in South China, in a four-year period there were 12 cases of orthograde intussusception, one of which was enteric and due to a submucous lipoma and the other 11 were ileocæcal. One of these 11 patients was 9 months old, a second 7 years and the remaining 9 were between the ages of 13 and 39. There was no cause apparent for the intussusception in any of the ileocæcal cases and swollen lymphoid tissue would not appear to be a satisfactory explanation for the 9 cases in the age group 13–39, as that tissue has diminished by then.

There is the further difficulty of why intussusception should occur in a retrograde direction. Best and Taylor (1955) stated that antiperistalsis is a normal occurrence in the duodenum beyond the cap and for a variable distance above the ileocæcal valve, but that with these exceptions peristalsis normally only travels in a distal direction. Samson Wright (1952) mentioned both the occasional occurrence of feeble retrograde waves arising near the hepatic flexure under normal conditions and also the occurrence of powerful retrograde movements in the colon in the presence of obstruction. Balfour (1918) recorded an interesting observation made during an operation performed by W. J. Mayo. After reducing a retrograde colo-colic intussusception associated with a malignant papilloma of the sigmoid, it was seen to recur with powerful anti-peristaltic contractions of the proximal sigmoid. If it is assumed that the tumour was responsible for initiating this abnormal retrograde peristalsis of the colon, there is still no explanation for its occurrence in an idiopathic case like the one I have reported. We do not know why idiopathic intussusception occurs nor what determines its direction. That the orthograde type is much the commoner accords with the normal direction of peristalsis. Retrograde peristalsis may occur more often than has yet been demonstrated in the descending and pelvic colon, where nearly all these intussusceptions originated.

SUMMARY

(1) A case of retrograde intussusception of the colon is described.

(2) This is the 15th case to be reported—9 being idiopathic and 6 secondary. In 13 of these cases the intussusception started in the pelvic or descending colon.

(3) The classification of retrograde intussusception of the colon and its ætiology are discussed.

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Section of Medicine

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[*January* 24, 1956]

DISCUSSION ON RECENT ADVANCES IN TREATMENT

Professor Andrew Wilson: *Morphine Antagonists*

To serve as a background for the discussion of recently discovered morphine antagonists I would like to refer to a case of morphine poisoning quoted by Binz (1895) sixty years ago:

"... The man was deeply cyanosed, especially as regards the face and hands; his respiration was very infrequent, his pulse slow, weak and irregular, the pupils extremely contracted, whilst there was profound insensibility, and the temperature in the rectum was 97·2° F. Recourse was had to artificial respiration, and 1 mg. of atropine was injected. At the end of half an hour no sign of improvement being visible, a further injection was given of 10 mg. of atropine. Fifteen minutes later the cyanosis had disappeared, the sounds of the heart were more regular, though the contractions still remained at 40 per minute. In the course of the next twenty minutes 10 mg. more were injected at different spots on the buttocks, and artificial respiration was continued. Within ten minutes more the pulse rose to 60, and the pupils regained their normal size; half an hour later the pupils were fully dilated, the heart-sounds normal, the pulse 80, but the patient was still comatose. Afterwards the nervous system gradually recovered its sensibility to external impressions. The following morning, twelve hours after the administration of these large doses of atropine, the condition of the pulse, pupils, and respiration was normal."

One of the significant features of this report is the scant reference to the return of normal respiration and the observation that after treatment for an hour and three-quarters the patient was still comatose despite the administration of 21 mg. of atropine sulphate. By contrast, the dramatic effect of nalorphine in counteracting the action of morphine on the dog, which will be described later, has naturally aroused much interest.

Compounds which antagonize morphine.—A number of compounds have been shown to antagonize various actions of morphine in a variety of species. Some of these compounds, for example nalorphine and levallorphan, are closely related to morphine in chemical structure. The substance WIN 7681 is a similar analogue of pethidine. Other compounds described by Shaw and Bentley (1949, 1952) which include diamino-phenylthiazole and a number of derivatives of 5-amino-acridine are not structurally related to morphine.

Other contributors to this discussion will consider the effects of diamino-phenylthiazole (Shaw and Shulman, 1955; McKeogh and Shaw, 1956). I propose to discuss only those drugs on which there is detailed clinical evidence and for this reason I shall focus attention on the effects of nalorphine and levallorphan.

Actions on animals.—Pharmacological investigations of these two compounds have been concerned in establishing (1) the action of the antagonist compared with its parent compound, and (2) the effects of the antagonist in preventing or abolishing the actions of the parent or of other similarly acting compounds. The evidence obtained with experimental animals is fairly consistent and clearly shows that nalorphine has analgesic activity which is much less than that of morphine; it initially stimulates but later depresses respiration but does not apparently produce cerebral excitement in the cat. Similar comparisons of levallorphan with levorphan have not been so fully reported.

There is general agreement that in a variety of species, nalorphine, when administered prior to morphine, prevents the actions typical of the latter drug but the amount of antagonist required depends on the particular action which is to be suppressed and on the species. For example Orahovats and his colleagues (1954) showed that in the dog, the dose of nalorphine which suppressed respiratory depression, nausea and vomiting and general depression due to morphine, without affecting analgesia, was in the proportion of one part of nalorphine (0·15 mg./kg.) to 14 parts of morphine (2·0 mg./kg.). In the rat, the dose ratio of nalorphine to morphine was 1 : 32.

Nalorphine also *reverses* the actions of morphine; a spectacular effect of this type is seen in the dog which has been given morphine. One or two minutes after an intravenous injection of nalorphine the animal quickly awakes and is able to walk and the respiratory depression, bradycardia and miosis cease. Nalorphine has also been shown to abolish the effects of other potent analgesic drugs such as methadone, dihydromorphinone (metopon), levorphan and 6-methyl-delta-6-desoxymorphinone (Orahovats *et al.*, 1955).

Levallorphan is more active than nalorphine in restoring to normal the respiratory depression produced in rats by levorphan, methadone, morphine and pethidine (Costa and Bonnycastle, 1955). In most cases the action of the antagonist is less prolonged than that of the analgesic. I shall not attempt to discuss the mode of action of these drugs. For of this

there is little fundamental knowledge. It has been suggested on the basis of their relation in chemical structure to that of morphine and levorphan that they act as competitive antagonists. There are a number of reasons which serve to cast doubt on this interpretation. One of the most important of these is that a competitive antagonist does not ordinarily produce an effect on the tissue with which it combines, but merely competes with another drug for a particular part of the cell for which each has an affinity. It is clear that nalorphine and levallorphan do not fulfil this condition.

Actions on human subjects.—The weak analgesic activity of nalorphine observed in animals has also been confirmed by clinical trial; Lasagna and Beecher (1954) found that the relief of post-operative pain after the subcutaneous injection of 5 mg. nalorphine was similar to that obtained with a placebo. When doses of 10 or 15 mg. nalorphine were given, the accompanying side-effects were so unpleasant that the therapeutic use of the drug as an analgesic was abandoned.

One of the most surprising results of investigations on normal subjects is that although nalorphine in doses of 2–10 mg. intravenously does not produce any significant effect on the respiration rate, it nevertheless depresses the respiratory minute volume. This effect has been repeatedly demonstrated when the subject inhales 5% carbon dioxide; under these conditions it has been shown that the reduction of respiratory minute volume is as great after 5 mg. nalorphine as it is after 10 mg. morphine. Levallorphan also has a similar action which Thomas and Tenney (1955) compared with levorphan.

It is clear that these morphine antagonists differ in this important feature, from the analeptic and respiratory stimulant drugs which have hitherto been used as antagonists. Indeed it is now apparent that an excessive amount of nalorphine or levallorphan may produce the opposite effect on respiration from that which is intended, and this emphasizes the importance of determining the optimum dose ratio of antagonist to analgesic. An illustration of this point may be taken from some of the earlier reports on nalorphine. The successful reversal of respiratory depression due to morphine reported by Eckenhoff and his colleagues (1952) was seen in two patients who were treated with nalorphine in proportional doses of nalorphine to morphine, 1 : 5·7 and 1 : 4·5. By contrast Payne (1954) had disturbing experiences when he used a dose ratio of 1 : 1·5. It is noteworthy that in each instance the authors did not observe any evidence of an awakening effect by the antagonist.

The possibility has been explored of combining the antagonist and analgesic in various proportions in order to provide analgesia without respiratory depression, but the investigations so far have been attended with little success. Lasagna and Beecher (1954) found that the combination of 2 mg. of nalorphine and 10 mg. of morphine (1 : 5) produced analgesia and side-effects indistinguishable from those seen after 10 mg. of morphine. Likewise when 5 mg. of nalorphine and 15 mg. of morphine (1 : 3) were injected together, the respiratory depression and subjective side-effects were similar to those obtained with 15 mg. of morphine.

Eckenhoff and his colleagues (1955) who injected intramuscularly levallorphan and levorphan in a dose ratio of 1 : 1 and 1 : 10 reported that they were unable to prevent respiratory depression normally produced by levorphan; this experience led them to conclude that this method of using the drugs in combination was not worth while.

There have been a number of other reports on the effects of mixtures of antagonist and analgesic but I shall discuss only two, each dealing with a different therapeutic problem.

In an attempt to reduce the side-effects of morphine as an analgesic in obstetrics, Cappe *et al.* (1953) injected patients in labour with a mixture of 15 mg. of nalorphine, 15 mg. of morphine and 0·4 mg. of hyoscine hydrobromide, a ratio of 1 : 1 and reported that all but one of the babies spontaneously breathed within two minutes of delivery. There was some evidence, however, of a decrease in the analgesic effect and a further report by Cappe and Pallin (1954) stated that with higher and lower doses of the drugs in the same dose ratio, there was intense hypnosis and analgesia. In experienced hands this method of using nalorphine and morphine in obstetrics may provide a successful therapeutic solution to the present disadvantages of morphine, but a controlled clinical trial, using the drugs in other ratios is clearly indicated.

The most successful therapeutic uses of the morphine antagonists have been in the treatment of neonatal asphyxia due to obstetric analgesic drugs, and in the management of poisoning by opium alkaloids or the new synthetic analgesic drugs, Reference has already been made to the administration of nalorphine to the mother before delivery; the other method of injecting this drug into the umbilical cord immediately after birth has given satisfactory results in all the reported studies (Eckenhoff *et al.* 1953; Adriani and Kerr 1953; Chalmers and Thornberry, 1954; Paterson and Prescott, 1954). The doses used in the investigations have ranged from 0·1–2·5 mg. but different mothers had been given different analgesic drugs, such as morphine, Omnopon or pethidine. Whilst no ill-effects were attributed to nalorphine, it is pertinent to know whether the dose of antagonist is in any

way related to the type of analgesic and the dose of it which had been given before delivery, for it is commonly accepted that the effects of pethidine are less disturbing to the fœtus than those of morphine.

There is well-substantiated evidence from animal experiments and from clinical investigations (Irwin and Seevers, 1952; Wikler and Carter, 1952) that subcutaneous injection of nalorphine produces, in morphine-addicted subjects, symptoms closely resembling those associated with the abrupt withdrawal of morphine. This method of revealing suspected addiction is not recommended. Interesting work has recently been reported on this subject by Isbell (quoted by Lasagna and Beecher, 1954) which has some bearing on the possible use of mixtures of nalorphine and morphine. Administration of these in a dose ratio of 1 : 5 to 1 : 10 to former addicts produces a milder degree of physical dependence than equivalent amounts of morphine alone. This observation may have some significance in relation to the prolonged administration of morphine, by preventing or delaying the onset of psychological or physical dependence and it would be interesting to know whether such mixtures have any influence on the development of tolerance.

Perhaps the most disappointing feature attending the treatment of morphine and related types of poisoning, by means of nalorphine, has been the failure of the patient to sit up and walk about, as had generally been expected from studies on the dog. Nevertheless those who have experience of this treatment have recognized the value of this drug in restoring satisfactory respiration despite the persistent drowsy state of their patients. The optimum dose of antagonist for this purpose is probably within the range of 10–20 mg. of nalorphine and of 3–5 mg. of levallorphan.

Further information is needed about the duration of actions of these antagonists in counteracting the effects of different analgesic drugs. In the management of poisoning, such information would facilitate the choice of antagonist; it would also provide a valuable guide to the frequency of administration.

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Dr. S. Locket: *Barbiturate Antagonists*

The existence of an effective barbiturate antagonist would be of more than mere academic interest. In England and Wales alone in 1954 we had 574 known deaths, and about 6,000 non-lethal cases of poisoning due to the barbiturate, and these figures are increasing annually (Locket, 1956). In many other western states, particularly certain Scandinavian countries, the situation is even more grim, poisoning by this group of drugs reaching relatively colossal proportions. In view of the wide difference of opinion on barbiturate antagonists as expressed in current writings I propose to use data relating to my own experience, and the few conclusions that these figures would seem to indicate to me.

My first group is a small group of 22 cases treated in an almost uniform manner, but receiving in addition the drug picrotoxin. Unfortunately, no blood barbiturate levels are available here. There were two deaths in this group and both were in patients who had taken large doses of phenobarbitone (7 grams and 10 grams). One death occurred on the second day after admission and one on the seventh day, and in both cases at autopsy the lungs were waterlogged. 12 patients of this group of 22 would fall into the most severe group in the simple classification used by me (Table I) (Locket and Angus, 1952).

The next group of 30 patients have received the two drugs bemegride and amiphenazole. These two substances have been introduced only recently for the treatment of barbiturate

TABLE I.—SIMPLE CLINICAL CLASSIFICATION OF DEGREE OF SEVERITY USED FOR BARBITURATE POISONING (ON ADMISSION)

I Mildest group Conscious	II Stupor	III Most severe Coma
Will respond by deliberate activity to a command (may be drowsy, restless, intoxicated, sleepy or sleeping)	Will not respond to command no matter how persistent. Reflex objection to therapeutic procedures particularly if they are painful. Eyes may open but no comprehension. B.P. —normal range. Respiration rate — above 12 per min. No cyanosis. Reflexes all ++	Unconscious; respiration rate usually below 10 per min.; cyanosis often present; areflexia frequent; B.P. often low and even unrecordable. Tone of musculature usually flaccid

poisoning (Shaw *et al.*, 1954) and therefore it is necessary to dwell at greater length on this group. Most of these patients had received 1·0 gram of bemegride and correspondingly 0·30 gram of amiphenazole. A few had received more than this, and a few less. 12 patients of this group of 30 would be classified in the more "severe" group. 2 who received these drugs died, and these 2 deaths illustrate the difficulty which so often occurs in fatal poisoning by these drugs, in deciding upon the actual immediate cause of death.

The first fatality was in a male aged 40 years, known to have a cerebral tumour and who was receiving sodium amylobarbitone regularly. On admission, in deep coma, he had a blood barbiturate level of 4·8 mg.% amylobarbitone. In treatment he received only a minimal quantity of bemegride and amiphenazole. In view of his past history, this therapy was discontinued. He died sixty hours after admission to hospital, and at autopsy was found to have a massive malignant glioma.

The second fatal case was a female patient aged 73 years who arrived in hospital at 8.20 p.m. having taken 2,400 mg. pentobarbitone sodium and 6,400 mg. carbromal less than two hours earlier. On admission the patient was unconscious and slightly cyanosed. Her breathing was noisy and snoring, but of fair depth and normal rate. Her blood pressure on admission was 180/110 mm.Hg. Most reflexes were absent, though both an ankle and triceps reflex jerk were just obtainable. After immediate gastric lavage, clearing of airway and administration of oxygen, administration of bemegride and amiphenazole was commenced, i.e. at 9.30 p.m. Some spontaneous limb movements occurred after the administration of 100 mg. of bemegride and 30 mg. of amiphenazole, and her breathing seemed deeper but not faster. After an hour, at about 10.30 p.m., when the patient had received 1,000 mg. of bemegride and 300 mg. of amiphenazole, the administration of these two drugs was stopped. It was noted that the diastolic pressure had fallen during this therapy to 60 mm.Hg, but the patient seemed more "active". An hour later, in view of her continuing deterioration, the drugs were recommenced, but as a further 250 mg. of bemegride and 75 mg. of amiphenazole produced no improvement they were discontinued. This patient died seven and a half hours later. In spite of the dose of pentobarbitone ingested, her blood level on admission was only 0·25 mg.% pentobarbitone and the level in her liver, at autopsy, was only very little higher (0·60 mg. per 100 grams).

It is interesting to speculate as to the cause of death in this last case. If early gastric lavage is presumed to have successfully removed most of the ingested pentobarbitone it must have removed most of the carbromal. Could the immediate cause of death have been the treatment given?

A few other cases in this group were of interest.

Case I.—Female, aged 48 years, admitted in coma due to the taking of sodium barbitone and possibly a quantity of chlorpromazine. She was not the clinical picture of profound barbiturate narcosis. On admission her blood barbiturate level as barbitone was 16 mg.%. She was given 150 mg. of bemegride and 45 mg. of amiphenazole, but without any effect on her state of unconsciousness, although limb movements occurred. About thirty-six hours later (her blood barbiturate level now being 11·2 mg.%), since she was still unconscious, though respiration, blood pressure and reflexes were all normal, she was given further injections totalling 1·0 gram of bemegride and 300 mg. of amiphenazole. This caused more spontaneous limb movements and head turning, and a ready response to painful stimuli. Nevertheless there was no evidence of any return of consciousness. Her blood pressure and respiration rate were unchanged. She recovered consciousness sixty hours later, i.e. ninety-six hours after admission.

Case II.—Female, aged 26 years, admitted in coma. She was given bemegride and amiphenazole and within ten minutes of cessation of their administration, though her condition was in general unchanged, she was definitely more cyanosed than before the drugs had been given, and her breathing was even shallower and slower. She recovered consciousness after thirty-six to forty hours. Her blood barbiturate level on admission was 1·0 mg.% of amylobarbitone.

Case III.—Female, aged 46 years, admitted in deep coma, cyanosed, all reflexes absent, blood pressure only just recordable, and respiration shallow and less than 8 per minute. After the administration of 900 mg. of bemegride and 270 mg. amiphenazole with no appreciable effect on the patient's state of consciousness, or respiration rate, nor the occurrence of any spontaneous movements, the case record then reads "Patient's general condition seems to be deteriorating steadily during this treatment. The systolic blood pressure, which was 120 mm.Hg at the commencement of treatment, has now fallen to 90 mm.Hg". The patient showed no further deterioration on discontinuing the drugs. The next day she was rousable. On admission her blood barbiturate level was 1·7 mg.% amylobarbitone.

Case IV.—Male, aged 33 years, a known epileptic, who on admission to hospital, after a known suicidal attempt, was unconscious and unrousable, slightly cyanosed with respirations less than 10 per minute, but of good volume. After he had received 100 mg. of bemegride and 30 mg. amiphenazole generalized convulsions occurred, but the patient remained unconscious. The administration of the two drugs was immediately stopped and the convulsions ceased within five minutes. This patient remained unconscious for a further four days. His blood barbiturate level on admission to hospital was 8·2 mg.% of phenobarbitone, and this level had fallen to 4·0 mg.% phenobarbitone on the day of recovery from coma.

TABLE II.—BLOOD BARBITURATE LEVELS

In relation to clinical classification of severity—in mg. per 100 ml. blood (on admission)

	Conscious I	Stupor II	Coma III
Amylobarb. ..	Less than 0·9	0·3 to 3·1 (Average 0·8)	0·3 to 6·5 (Average 1·8)
Butobarb. ..	Less than 1·0	0·5 to 1·8 (Average 1·4)	0·8 to 3·5 (Average 2·1)
Phenobarb. ..	Less than 6·7 (85% of 140 readings were below 3·0)	2·4 to 10·4 (Average 4·3)	4·0 to 15·2 (Average 8·0)
Barbitone	*Less than 6·0	5·2 to 10·0 *(Average 6·8)	11·0 to 17·0 (Average 13·4)
Pentobarb. ..	Less than 0·75	0·25 to 1·1	0·45 to 1·8
Secobarb... ..	Less than 1·0	0·3 to 1·5 (Average 1·0)	0·7 to 2·0

*One patient in each of these had also taken amytal (Group I 3·1 and Group II 5·2)

Table II gives the blood levels for corresponding degrees of clinical severity, based on blood levels in more than 500 of our cases.

For comparison with the data given already on bemegride and amiphenazole, I give some comparable information on my last 1,000 admitted cases of barbiturate poisoning treated without analeptics, antagonists or convulsant drugs (Table III).

TABLE III.—GROUPS OF PATIENTS TREATED

Picrotoxin group	22 patients	12 severe ("Comatose" group)	2 deaths
Bemegride / Amiphenazole } group	30 patients	12 severe	2 deaths
"Token" or single injection group	81 patients	25 severe	2 deaths
No analeptic or "specific" drug	1,000 patients*	326 severe	18 deaths

*In this series we had a run of 134 successive cases with no deaths and then 3 deaths in the next 5 cases.

About 40 patients had received elsewhere a single, or less often, two injections, or "token" doses of picrotoxin and about an equal number had received nikethamide. These injections did not seem to influence the course of the intoxication in any way.

Recently some 12 cases included in this group have been given an intravenous infusion of *l*-noradrenaline to raise the blood pressure. There were no very obvious disadvantages in its use.

The group of 1,000 cases includes many cases of which the following are illustrative:

Case I.—A female patient aged 60 years admitted in a drowsy condition but in full possession of all her faculties with a blood phenobarbitone level of 6·7 mg.%.

Case II.—A female epileptic aged 27 years, admitted in coma with a blood barbiturate level of 11·8 mg.% phenobarbitone. She recovered from her coma on the seventh day when her blood level had fallen to 6·0 mg.% of phenobarbitone.

Case III.—A female aged 66 years, comatose on admission with a blood barbiturate level of 11·5 mg.% barbitone who had recovered and entered the stuporous state in twenty-four hours when her blood level had fallen to 10 mg. of barbitone.

The fatal cases in this group presented their usual crop of problems of which the following case is an example:

Female, aged 65 years, who, after taking phenobarbitone and aspirin was admitted with anuria and in deep coma. Blood urea was 100 mg.% on admission and this had risen to 210 mg.% on the fourth day just before she died. Her blood barbiturate level was 4·0 mg.% phenobarbitone on admission but increased to 10·9 mg.% phenobarbitone on the fourth day just before she died. Her blood salicylate level was 34 mg.%.

I have now also seen a large number of patients who on admission are collapsed, with bradypnœa and cyanosis and areflexia, yet have regained consciousness rapidly following adequate ventilation and oxygenation. The barbiturate taken was invariably one of the "quick-acting" variety and the blood barbiturate level on admission was usually low.

If you believe the use of an "antagonist" to be life-saving, it cannot be withheld for twenty-four hours and reserved only for those patients still unconscious at this stage. The dilemma is that a patient given a clinical classification suggestive of great initial severity may nevertheless show rapid recovery of consciousness with purely expectant treatment, yet on the other hand blood barbiturate levels, unless very high, are no real criterion of severity, since patients with relatively low blood levels may die, whereas others in all respects identical and with higher blood barbiturate levels may nevertheless not even be more than stuporous.

We use "antidote" as the name for any substance believed to have an action from the time of its administration which would be advantageous to the receiving organism in that it is directed against that of another substance, *already administered* and almost invariably toxic. The action of the antidote may be either upon the poison or upon the organism.

This wide and very general usage of the term "antidote" covers the more restricted and more limited meaning of the term "antagonist" when it is applied to a poison.

To most, the term "antagonist" implies specificity of a kind not implied by the term "antidote," though this term too carries a less-defined implication of specificity. An antagonist has no action on the toxic agent itself, but by inducing alterations in the state of the receiving organism it prevents the development of pharmacological activity by that toxic agent and

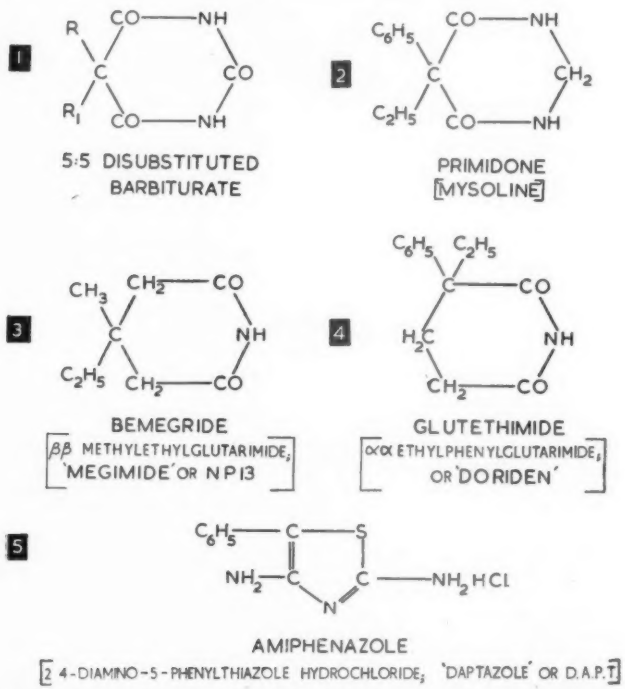

FIG. 1.—For comparison the structure of Glutethimide, a new hypnotic drug, and Primidone, a non-hypnotic anti-epileptic drug, are given.

makes any toxic changes recede, if they have already occurred. Originally the term antagonist implied "reciprocity" some competition between antagonist and agonist (i.e. toxic agent) for a particular cellular group or a specific site of action in the organism. However, this rather rigid nomenclature has recently been considerably relaxed and the term now covers almost the same range as "antidote" and is used just as vaguely.

The terms "antidote" and "antagonist" do not imply or even necessitate any chemical identity or chemical reciprocity with the toxic agent (Fig. 1).

An awakening agent, with no effect on the respiratory centre would be useless, since depression of the respiratory centre is related to the blood level of barbiturate, and therefore to the degree of consciousness only in so far as this too is related to the blood barbiturate level, and no antagonist or antidote has yet been claimed to lower this level.

In my opinion, and as a result of my own experience, there is not as yet available a barbiturate antagonist, in any reasonable interpretation of this term (excluding oxygen and the antibiotics, particularly penicillin), capable of having any appreciable specific effect upon the course of barbiturate intoxication. On the contrary it would seem to me that some of our results with bemegride and amiphenazole may show them to be distinctly disadvantageous in the more precariously balanced comatose patients, that is those precariously balanced between recovery and death.

Summary.—The high frequency of fatal and non-fatal cases of barbiturate poisoning makes the discovery of a barbiturate antagonist more than of theoretical interest. In 1,000 successive cases of barbiturate poisoning (326 severe cases) treated without any current "antagonists" there were 18 deaths. This group when compared with 2 deaths in 22 cases (12 severe) treated with picrotoxin, 2 deaths in 30 patients (12 severe) treated with bemegride and amiphenazole and 2 deaths in 81 patients (25 severe) receiving single injections of nikethamide and similar substances leaves no doubt that these substances are not antagonists to the barbiturates. In fact there would seem to be some evidence to suggest that the use of bemegride and amiphenazole may be disadvantageous.

I am most grateful to my collaborator on toxicological problems, Dr. W. S. M. Grieve, Biochemist at Oldchurch Hospital, Romford, who was responsible for all the blood barbiturate estimations utilized in this communication.

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Dr. Denis Williams: *Treatment of Epilepsy with Mysoline*

Until the hydantoins were introduced by Merritt some twenty years ago the medical treatment of epilepsy consisted of the control of convulsions by sedative substances—the bromides and barbiturates mainly, and the modification of *petit mal* in childhood by altering the pH of the body with the unpleasant ketogenic diet.

With the introduction of new families of therapeutic chemicals there has been a need to recognize the exact form of the epileptic disturbance, both from the phenomenon seen or experienced in the attack, and from the changes seen in the EEG, for substances which reduce convulsive activity may aggravate *petit mal*. It is odd that in this regard there may be a species difference so that Tridione, specifically effective in *petit mal* in man, is an anticonvulsant in some animals. The most difficult distinction is between the *petit mal* of childhood and brief focal epileptic attacks which may clinically be indistinguishable from them, but which are quite distinct in their EEG characteristics, if the physician is fortunate enough to record an actual attack.

In considering the usefulness of primidone (Mysoline) therefore, we must remember to deal with symptomatic and constitutional epilepsy separately, and to divide the patients into those with *grand mal*, focal attacks, *petit mal*, or mixed forms.

The effectiveness of primidone was demonstrated by Yule Bogue in the Imperial Chemical Industries' Laboratories in 1949 and the results published in 1953. In 1952 Handley and Stewart reported the effects of this substance when used in 40 patients in an epileptic colony. All the patients had been resistant to other anticonvulsants, and yet attacks were reduced in 80%, and ceased in 30%. They found little toxic effect, but commented that the substance was much more effective in patients with apparently constitutional *grand mal* than in those with symptomatic epilepsy. Several more reports soon followed. Whitty (1953) found improvement in 49 of 70 cases of epilepsy and was gratified that those in the "psychomotor" group, so often resistant to treatment, were benefited, and that toxic effects were mild. Nathan (1954) used the substance in 21 patients with symptomatic epilepsy who

had failed completely to respond to other anti-convulsants, and found that nearly half (43%) were improved. Lyons and Liversedge (1954) obtained a similar response in 44 out-patients. Sharpe (1954) reported that major fits were reduced in nearly half of a group of 38 mental defectives, but found no improvement in *petit mal*. Briggs and Tucker (1954) thought, however, that *petit mal* in childhood was definitely ameliorated. Later reports have been summarized elsewhere, and they all showed that primidone was a valuable addition to the treatment of epilepsy.

Except in *petit mal* of childhood phenobarbitone remains the first choice as an anti-convulsant in this country. It is often effective, it is well tried, safe, and has few and infrequent side-effects. Its main disadvantage is that some patients become exceedingly drowsy while taking it, and do not adjust to that effect. It is my practice to use phenobarbitone first, and if for any reason that is inadequate, to add phenytoin sodium in increasing doses. If treatment is still inadequate, I now use Mysoline, but I do not use it, as I do the hydantoins, with phenobarbitone, for the combination of both nearly always causes intolerable drowsiness and lassitude, not necessarily found with either substance alone. This may be because of their similar chemical formula.

My colleagues at the National Hospital and I have collected evidence on about one hundred out-patient epileptics, and the results are seen in Tables I, II and III.

TABLE I.—94 EPILEPTIC OUT-PATIENTS

Children	24%
Constitutional epilepsy	85%
Grand mal	87%
+ *petit mal*	42%
Focal only	13%

All had prolonged barbiturates and hydantoins

TABLE II.—MYSOLINE GIVEN TO 94 OUT-PATIENTS

Mysoline alone in	5%
For Less than 6 months	22%
from 6 to 12 months	27%
from 1 to 2 years	31%
over 2 years	20%

TABLE III.—RESULTS WITH MYSOLINE IN 94 OUT-PATIENTS.

No further attacks	15%
Improvement	49%
No change	25%
Worse (including toxic effects)	11%
Toxic symptoms in	17%
Mysoline stopped in	13%

All these patients were living at home, most were working, and all in good general health. The majority were thought to have constitutional epilepsy and most were adults. All had had fits for many years and, because of this they had all had phenobarbitone, other barbiturates, phenytoin sodium, or phenyl-methyl-ethyl-hydantoin. Some had had Tridione, bromides, and other substances. Because of the choice of therapy I have already outlined they were all people whose fits had not been controlled by persistent, and I think conscientious, use of other anticonvulsants. There was no other alteration in management or treatment on commencing Mysoline, beyond reduction of other anticonvulsants in some cases.

It will be seen that attacks stopped up to the time of this report, in a sixth of the patients, and were improved, often greatly, in another half. There was some improvement in two-thirds. These figures are a little better than had been my impression from nearly three years use of Mysoline, but perhaps the consistent failures on the doorstep are more evident than the more silent successes.

The general impression has been that *grand mal* attacks without local origin or evident cause respond most satisfactorily to Mysoline, that focal attacks of all kinds may respond occasionally, and that Mysoline is not of value in pure juvenile *petit mal*. In the present series, 3 of the 12 patients with focal epilepsy were improved, and there was no improvement in the other nine. An equal number of patients with mixed *grand mal* and *petit mal* were and were not improved, but the improvement referred to the *grand mal*. I have no figures on *petit mal* because I continue to use Tridione as the substance of choice.

Apart from occasional idiosyncrasy with rashes and in one case dramatic coma on a test dose of 0·12 gram in a man known to be sensitive, with therapeutic doses of three to six 0·25 gram tablets a day, the most worrying side-effects are drowsiness, slowness, and mild ataxia, potentiated by phenobarbitone, but patients usually say that they are more alert on Mysoline than other anticonvulsants. Nausea and occasionally vomiting may make continuation impossible. Routine white blood counts are not done in the National Hospital, and as far as I know we have had no trouble of this sort with many hundreds of patients. Children sometimes get restless and obstreperous on Mysoline, but I think that this is when the fits are controlled, and it may not be due directly to the Mysoline.

Primidone (Mysoline) has added to the help we can give patients with epilepsy and fortunately it often helps those whose fits do not respond to other anti-convulsants.

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Dr. R. M. Mason: *Benemid*

The production of a sustained uricosuric effect represents, I believe, an important advance in our treatment of gout—the first real advance since colchicine first came into use some fifteen centuries ago. I would add that we also have some understanding of how it works, which is more than one can say for colchicine, whose mode of action in gout still remains totally obscure, but which still holds its place as the drug of choice for the acute paroxysm. The discovery of probenecid was accidental and arose from the coincidental finding in 1948 (Wolfson *et al.*) that caronamide increased uric acid excretion in normal subjects, but, because of its side-effects, its use was not really practicable. However, a new benzoic acid derivative, probenecid, p-(di-n-propylsulphamyl)-benzoic acid, with a formula structurally related to caronamide was found to have a similar effect in blocking the tubular secretion of some substances such as penicillin, para-amino-salicylic acid, and para-amino-hippuric acid (Boger *et al.*, 1950; Boger and Crosson, 1950); Gutman and Yu (1950) and others showed that it also interferes with renal tubular mechanisms bringing about the reabsorption of urate from the glomerular fluid. Its toxicity is low, amounting to no more that occasional gastro-intestinal disturbance, drug rash, and, rarely, an acute sensitivity reaction. Boger and Strickland (1955), analysing 2,502 cases treated with probenecid found that gastro-intestinal upsets occurred in 3%, a rash in just over 1%, and a hypersensitivity reaction only in 0·3%. Renal colic can, of course, be produced by the precipitation of uric acid crystals in the urine, but this can be avoided by maintaining a high fluid intake, and ensuring that the urine is alkaline.

Probenecid is quite different from cinchopen (Atophan), which is a poison to the kidneys and liver. It is not the only, nor even the first or most efficient uricosuric substance, apart from cinchophen. Jennings in 1937 recommended high dosage sodium salicylate administration, but for some reason thought that intermittent dosage three or four days a week would be sufficient. Later workers, however (Bauer and Klemperer, 1947; Marson, 1953), concluded that equivalent urate retention occurs during the intervals. Marson (1953, 1954, 1955) has certainly shown that sodium salicylate in a dose of 60 to 120 grains a day is more effective that probenecid, reducing the plasma level to 50%–60% of pre-treatment values, as compared with probenecid which, on the average reduces it to between 60% and 70% only. Nevertheless the prescription of 90 grains of sodium salicylate a day indefinitely is formidable to a patient and is rarely acceptable. If aspirin is preferred, then this is equivalent to 18 tablets of aspirin daily for the rest of the patient's life.

The problem of the treatment of gout is twofold. There is a silent asymptomatic natural history, punctuated by acute paroxysms and secondly the relatively cold, often symptomless deposition of urate. This may, however, give rise to chronic joint symptoms, urate being deposited, not only in joints, but in other tissues, especially the kidneys.

In acute gout colchicine has a specific effect but it has no influence whatsoever on blood levels, nor is there much in the way of observable changes in blood levels in association with the acute attack (Jacobson, 1938; Mason, 1951). On the other hand uricosuric drugs are ineffective in relieving the individual paroxysm; yet we must accept that hyperuricæmia, and both acute and chronic gout, bear a general relationship to each other.

Against this background let us see that happens when probenecid is given.

Case I.—This patient was a taxi-driver, with a long history of gout; his attacks had become polyarticular with fairly complete intervals of remission. His serum uric acid was running at between 8 and 9 mg.%, and his urinary output of uric acid at 745 mg. per twenty-four hours. On giving him 2 grams probenecid a day, there was an immediate rise in the urinary output to 1,500 mg. in the twenty-four hours, slowly falling off as the serum uric acid fell, in this case to well below normal levels. But at the point where his blood level had fallen to a lower value than it had been for many years, he had an attack of gout. Soon afterwards he had a further and very severe polyarticular attack and on readmission one month later, his serum uric acid was 2·3 mg.% and his output still slightly above pretreatment levels (fig. 1).

This case illustrates this curious phenomenon of acute attacks when the blood level has been brought sharply to normal.

From the practical point of view, one can usually avoid this complication by giving small initial doses. I usually give 0·5 gram daily for the first two weeks, 1 gram for the second two weeks, 1·5 grams for a further two weeks, and then repeat the serum uric acid

(fig. 1). If it has fallen to 60% of pre-treatment values, then this would be the maintenance dose. If a further fall seems desirable, the dose can be increased to 2 grams daily.

Can probenecid be used in the presence of renal failure? I believe it can, and there seems general agreement on this, although it may be less effective.

One such patient whose renal function was grossly impaired, his urea clearance being 20% of average normal, and his blood urea 70 mg.% has been studied in detail (Mason,

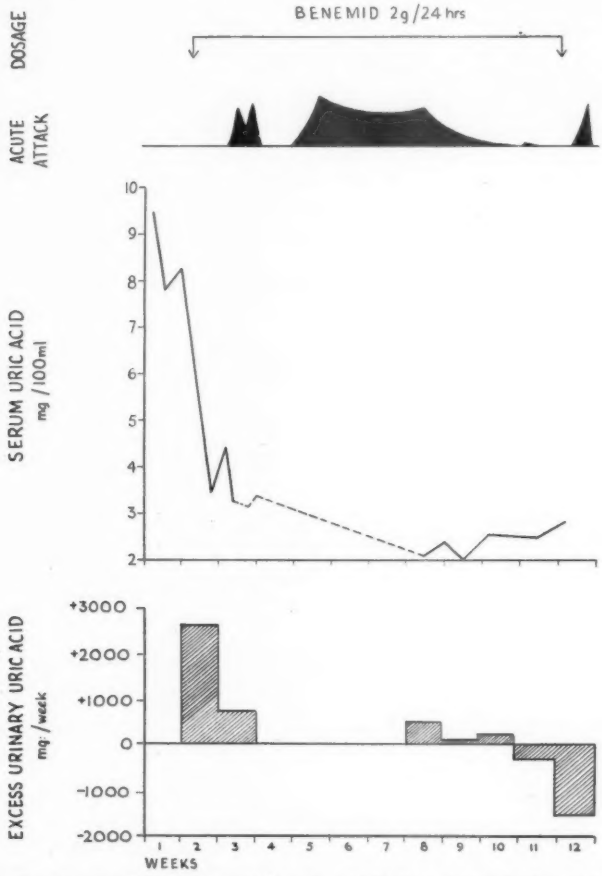

FIG. 1 (*Case I*).—Serum uric acid and urinary uric acid findings during twelve weeks' observation (mean urinary uric acid during control period, 745 mg./twenty-four hours, is shown as ± mean of control output in mg. per week). (Reproduced from the *Annals of Rheumatic Diseases*, by kind permission).

1954). He had an acute attack during the control period, with a considerable rise in the serum uric acid level. At its peak, 12·5 mg.%, this patient's general condition became a source of anxiety and treatment could not be withheld. He was, therefore, given both probenecid and colchicine. Subsequently his blood level fell to below 6 mg.%. It was observed, however, that the blood urea rose considerably to a maximum of 118 mg.% during and just after the acute attack. I suspect that the changes in urate values are more a reflection of his renal failure than a direct and specific association with the acute attack.

Turning to the long-term effects, there is little doubt but that despite this early tendency to precipitate an acute attack, the maintenance of a prolonged uricosuria with a lowering of blood levels does gradually lead to a diminution in the frequency and severity of attacks, although this may take many months.

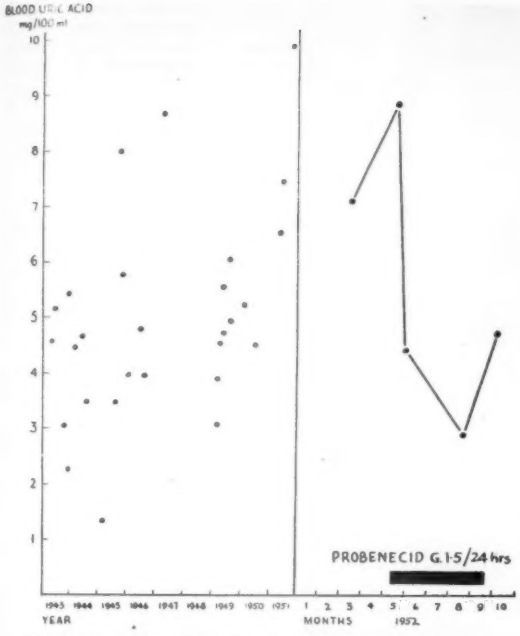

FIG. 2 (*Case II*).—Serial blood uric acid readings in a case of gout, showing the effect of probenecid 1·5 grams/twenty-four hours. (Reproduced from the *Postgraduate Medical Journal*, by kind permission).

Case II (Fig. 2).—This patient had a long history of gout, and, being a medical practitioner, had kept a regular watch on his blood level. This shows a fairly wide scatter, different laboratories being no doubt partly responsible for this, but there is observable a steady climb over the years until, in 1951, three readings of 6·5, 7·4 and 10 mg.% were found. After probenecid administration there was a rapid fall to roughly what he had been ten years previously. This has remained much the same three years later, his last reading being 4·8 mg.% a few weeks ago. He has had one attack following pneumonia only, and is taking as little as 0·5 gram probenecid daily (Mason, 1955).

Case III.—Fig. 3 illustrates the effect of probenecid on a licensee, whose history goes back twenty-five years, with gradually increasing frequency of attacks, becoming polyarticular with chronic tophaceous gout developing. The diagnosis was only made in 1953, however, when his plasma uric acid was between 8 and 9 mg.%. He was treated with colchicine and probenecid 2 grams/twenty-four hours. A few months later amputation of one toe was carried out because of a chronically infected tophus. This was fol-

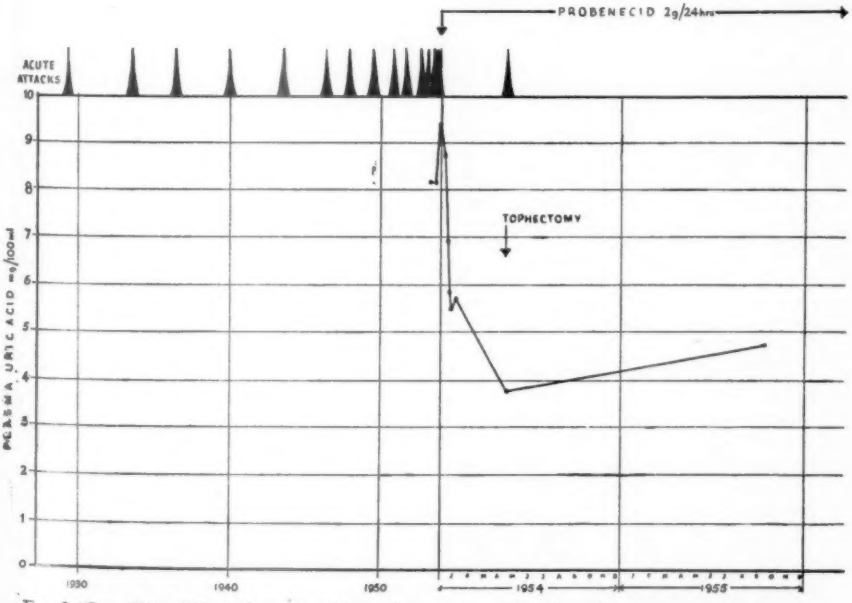

FIG. 3 (*Case III*).—Effect of probenecid on plasma uric acid and on the natural history of gout.

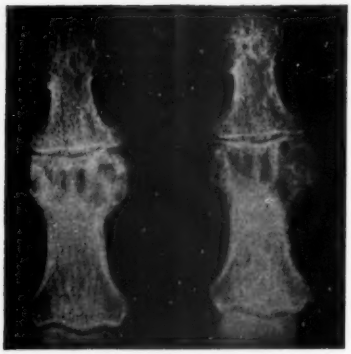

FIG. 4 (*Case III*).—Change in the radiological appearance of a tophaceous interphalangeal joint. L, after 18 months' continuous probenecid administration. R, before treatment for comparison.

lowed by a post-operative attack of gout, but he has remained entirely free of symptoms since then. His tophi have diminished in size and his olecranon bursæ have also become much smaller. Radiological improvement is observable even after eighteen months (Fig. 4).

In conclusion there are three points which seem to me to be important. Firstly, at what stage in the natural history of the disease should one begin long-term uricosuric therapy?

If we regard the disease as occurring in five clearly-defined stages: I. Asymptomatic hyperuricæmia. II. Acute monarticular attacks with complete remissions. III. Polyarticular attacks, with complete remissions. IV. Acute polyarticular attacks with incomplete remissions. Tophi appear. V. Chronic gouty arthritis—or chronic tophaceous gout.

It seems that we must try and prevent the patient reaching stage IV, that is to say the point at which deposition of urate begins to declare itself. How long before that will depend on the rate at which the disease is developing. In stage II, for instance, many years may elapse between attacks and we would be doing the patient a disservice by starting him off on a lifetime of medication. So much depends on the patient's occupation, age, and on a number of other factors. No hard and fast rules can apply. In principle, however, the sooner the patient's uric acid level is brought near normal, the better.

Secondly, should we advise the patient to have salicylate or probenecid? We must accept that sodium salicylate or aspirin in a dose of 90 grains a day is about 10% more effective than probenecid in lowering the blood levels. If there is very marked hyperuricæmia, above 10 mg.%, then sodium salicylate ought to be recommended, and some patients may accept it. If probenecid proves inadequate, there are grounds for recommending sodium salicylate, or if a patient is sensitive to it. We must also bear in mind the difference in cost. Probenecid costs 13s. 0d. a week in a dose of 2 grams a day. Sodium salicylate 90 grains daily costs 1s. 9d. a week.

Finally, there is this observation that acute attacks of gout may be precipitated when the blood level has been brought to normal. This suggests that a possible explanation is that uric acid itself is not responsible for the acute paroxysm of gout, but that it is a precursor which subsequently forms uric acid.

Although I would resist the temptation to join Bartels (1955) who wrote a paper entitled "Gout now amenable to control" using probenecid, and Marson (1955) who entitled a paper "The complete relief of gout" using salicylate, we are to-day in a position to tell a patient with gout that he is fortunate to have one of the diseases for which modern drugs will provide very satisfactory relief—the very first of the arthritides to be preventable—and, what is more, without imposing on him those severe restrictions of diet and drink which have hitherto been traditional.

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Section of Pædiatrics

President—J. VERNON BRAITHWAITE, M.D., F.R.C.P.

[*November* 25, 1955]

Two Cases of Hæmangio-endothelioma with Hæmorrhage, Thrombocytopenia and Bone Changes.—A. WHITE FRANKLIN, F.R.C.P.

(1) M. C., female, born at Queen Charlotte's Maternity Hospital 1.7.55 at full term, weighing 8 lb. 6 oz. Progress was normal, but on the eleventh day a small induration was noted in the right interscapular area. This gradually increased in size and because there was some redness of the skin over it, a diagnosis of skin infection was made, and Terramycin was given by mouth. When seen on the 27th day it was smaller, there was no redness and the swelling was about 1 in. across, freely movable in the subcutaneous tissues, attached to the skin. Aged 2 months the swelling suddenly enlarged with discoloration of the skin, increasing in size and extent, and when seen three days later there was a large red indurated area occupying the interscapular region mainly on the right. The appearance was of a subcutaneous hæmorrhage with some outlying petechiæ.

Admitted to St. Bartholomew's Hospital 6.9.55, weight 11 lb. 9 oz. No other abnormality noted. Hb 66%. W.B.C. 9,800, normal differential. Bleeding time over 20 minutes, clotting time 4 minutes, platelets 60,000 per c.mm. Spine X-ray (14.9.55 and 22.9.55) showed a defect of the right side of the body of D.9 (Fig. 1). Deep X-ray of the mass began

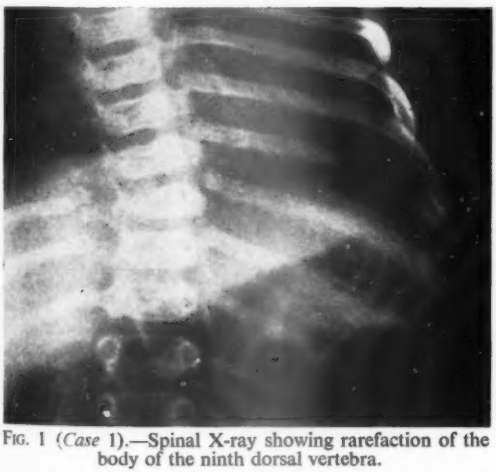


FIG. 1 (*Case* 1).—Spinal X-ray showing rarefaction of the body of the ninth dorsal vertebra.

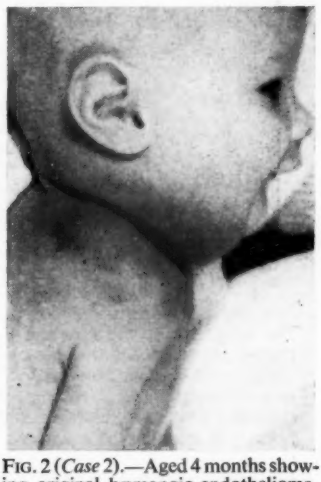


FIG. 2 (*Case* 2).—Aged 4 months showing original hæmangio-endothelioma.

20.9.55, but was omitted on 4.10.55 because the platelets had fallen from over 100,000 to 46,000 per c.mm. There was some slight diminution in the size of the swelling. The spleen became palpable and also a left axillary lymph node. Tibial marrow (Dr. H. F. Brewer), 21.10.55: numerous normal megakaryocytes. Dr. Storey reported no platelet agglutination against two group O platelet suspensions (26.10.55). Dr. I. G. Williams therefore agreed to recommence X-ray treatment on 31.10.55. This time the effect on the swelling was very striking and with its decrease the platelets have steadily risen to 226,000/c.mm.

Biopsy of the firm edge of the swelling (23.9.55) confirmed the diagnosis of hæmangio-endothelioma with local malignant infiltration.

The parents live in Gibraltar. There is one 6-year-old sister. There is no family history of bleeding, excessive bruising or of birth marks.

(2) I. K., male, born 24.12.46, is shown as a follow-up case with a history of hæmangio-endothelioma in the right cervical region, thrombocytopenia, and hæmorrhage, responding

to X-ray treatment. Bone changes are present in X-rays of the right clavicle at 9 days and remain with involvement of the upper end of the right humerus at 8 years. The history began with a large hæmorrhage into the right side of the neck at 6 days. This enlarged rapidly and then diminished, but at 3 months there was a sudden enlargement leading to anæmia and respiratory distress; platelets numbered 13,750 per c.mm. Fig. 2 shows the patient at 4 months. Following blood transfusion a little X-ray treatment at this time caused no noticeable change but three weeks after the end of the treatment many small hæmangiomata appeared on the shins. These disappeared spontaneously and are regarded as benign metastases. At 10 months the platelets were only 10,000 per c.mm. and the mass seemed to be enlarging once more; a second course of X-ray treatment was followed by great improvement but once again transient metastases appeared.

His case was fully reported (*Arch. Dis. Childh.*, 1953, **28**, 490) up to the age of 6 years. At that time the hæmangio-endothelioma had disappeared, his blood count including platelets had been normal from the age of 3 years, but he had limitation of movement of the right shoulder-joint with atrophy of the skin and subcutaneous tissues in the right side of the neck and bone rarefaction in the X-ray involving the outer end of the right clavicle and the upper end of the right humerus (Fig. 3).

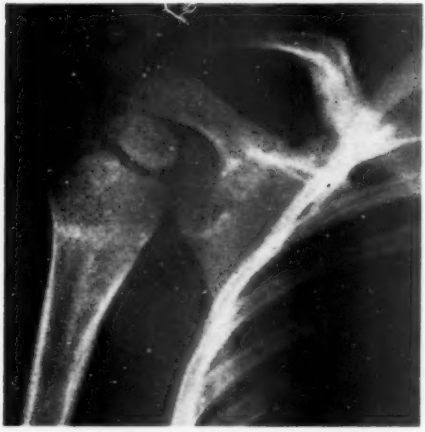


FIG. 3 (*Case* 2).—Shoulder X-ray, aged 2 years, showing rarefaction of bone.

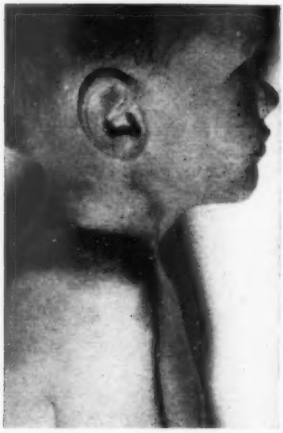


FIG. 4 (*Case* 2).—Aged 7¾ years showing fibrosarcoma in the neck.

In July 1954 (aged 7½) he developed a hard swelling in the area of his original lesion. This was fixed to the skin and to deeper structure. Blood counts (repeated) showed normal values. Platelets 268,000 per c.mm. Bleeding, clotting, prothrombin tissues were normal.

Biopsy (Mr. J. P. Hosford)*: Specimen of skin* shows prominent vascular spaces suggestive of a hæmangioma. *Specimen from tumour* shows the nodule to be composed of moderately cellular fibrous tissue which is extending into and apparently destroying voluntary muscle fibres. A number of thin-walled vascular spaces are included in the fibrous tissue. The appearances would suggest that there has been some differentiation of this neoplasm towards a connective tissue tumour—possibly related to the X-ray therapy (Dr. R. J. R. Cureton).

After a five-week course of deep X-ray treatment (250 kV, total 2,100 r) to the right side of the neck, the tumour lessened in size. One year later (November 1955) the general condition remains good and the hard tumour can still be felt although it is somewhat smaller (Fig. 4). Aged 8¾ years, height is 45½ in. and weight 44 lb. 10 oz.

Discussion.—These cases are reported in the belief that a special syndrome exists of which *Case* 1 is the thirteenth reported in the English and American literature. All had a tumour or a diagnosed hæmangioma at birth or within the first two months of life, the cases coming under notice on account of hæmorrhage into the mass in the period between 6 days and 5 months of age. All have had thrombocytopenia, but all survivors have in the end a normal blood count. Bone changes were present in 5 cases, of which these are 2, in 3 bones are described as radiologically normal, in 5 no X-rays were taken. 3 have died, 1 of infection at 6 months, 1 of hæmorrhage and asphyxia at 5 weeks and one of hæmothorax at 21 months. Splenectomy in 4 cases produced neither decrease in the tumour nor increase in the platelets. Deep X-ray treatment or radium has been used in 8 cases and was followed by improvement where adequate doses were given. 3 showed slow spontaneous improvement. Whereas in a few the platelets have risen as the tumour disappeared, there

has been a time lag in others. *Case* 2 who had benign hæmangiomatous metastases proved by biopsy has now a fibrosarcoma on the site of the original lesion. No other case is recorded over so long a period.

These appear to be cases of true vascular neoplasm of moderate malignancy, present at or soon after birth, with power of local infiltration, but also of spontaneous regression. They are liable to be the site for acute hæmorrhage with thrombocytopenia, anæmia and shock from blood loss, or severe complications from pressure on neighbouring structures. The treatment is blood transfusion followed by local deep X-ray therapy. Whether removal of the clinically apparent hæmangioma would prevent hæmorrhage and thrombocytopenia is not known. With a "hæmangioma" and thrombocytopenia, and plenty of megakaryocytes in marrow smears, local deep X-ray treatment should be seriously considered.

Staphylococcal Septicæmia with Meningitis, Endocarditis and Multiple Embolic Phenomena. Failure to Respond to Massive and Combined Antibiotic Therapy until Cortisone Added.—S. D. V. WELLER, M.D., M.R.C.P.

G. K., girl aged 5. Admitted January 21, 1955, after one week's cough, one day's fever, rash and delirium. Temperature 104·8° F.: septic purpura on feet and hands with gangrene of one toe and tip of one finger: photophobia: stiff neck: heart (and chest X-ray) normal. Cultures from blood, purulent C.S.F. and skin bulla all grew *Staphylococcus aureus*, fully sensitive to penicillin, streptomycin, Terramycin, erythromycin and Chloromycetin.

Treatment and progress.—All these antibiotics used in sequence, in high dosages, without effect, except that meningitis cleared promptly. Skin emboli continued, and heart murmur appeared on 3rd day, with bloody diarrhœa lasting eight days. At suggestion of Professor L. P. Garrod, combined treatment with penicillin in huge doses (24 million units per day) and streptomycin (0 5 gram per day) was instituted from 5th day. On 8th day, sudden præcordial pain and collapse suggested coronary embolism causing myocardial infarction; subsequent pericardial rub and rapid cardiac enlargement with congestive failure supported this impression (*see* Fig. 1).

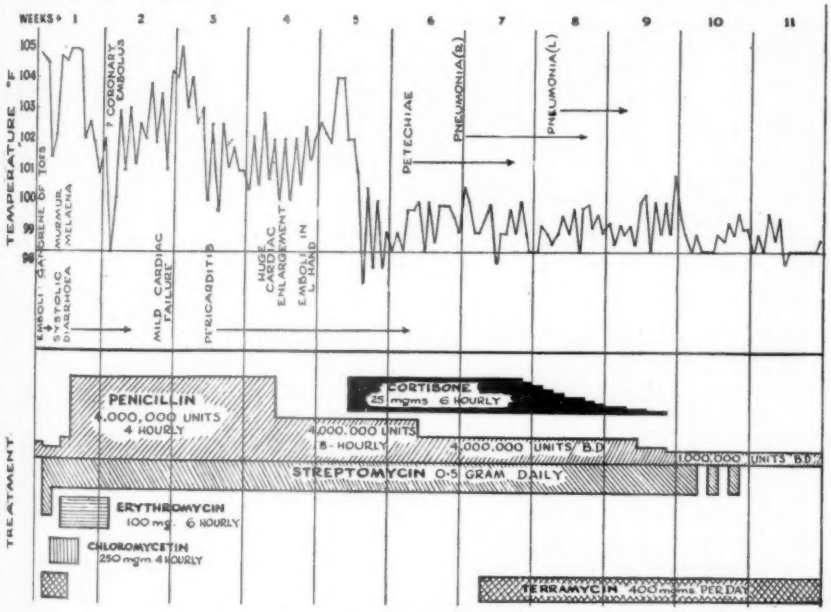


FIG. 1.—G. K., 5½ years. Staphylococcal septicæmia.

After three weeks, penicillin reduced to 12 million units per day in view of poor response and injection difficulties.

Cortisone started on 32nd day with immediate general improvement and fall of temperature, though petechiæ continued to appear. Massive bilateral pneumonia (without fever) developed in spite of antibiotics, demanding Terramycin. Cortisone and then all antibiotics tailed off from 45th to 91st day. Terramycin restarted because of alteration of

heart murmurs, replaced by erythromycin because of thrush and then by Sulphatriad for another pneumonia. Discharged 20.6.55 (after five months) with infection apparently eradicated but in mild congestive heart failure with large heart, apical systolic thrill and murmur, large liver and sacral œdema (possibly due to local reaction to injections into her scarred and nodular buttocks). The left tarsal scaphoid showed a small central sclerotic focus ? infarct.

Further progress (27.6.55).—Gross congestive failure with widespread œdema and ascites. Dramatic improvement with rapid digitalization (1·5 mg. Digoxin in first day) and Mercloran. Virtually uninterrupted progress in spite of sterile abscesses in buttock.

Present condition.—Excellent general health. Heart size and shape normal. Activity normal (full school day with games). Soft apical murmur persists. Liver normal. Left tarsal scaphoid now normal. Has been off Digoxin for six weeks.

Discussion.—The main interest of this case is the effect of cortisone in an infection which should from *in vitro* tests have responded rapidly to the antibiotics used—and which did in fact so respond at all recognized and accessible sites (meningeal and peripheral). The function of cortisone is presumably to reduce the "protective" action of local tissue response and thus expose the bacterium to the direct attack of antibiotics. The dangers of the treatment are illustrated by the development of pneumonia in spite of the antibiotic cover: the fear of increasing cardiac embarrassment was not fulfilled.

The remarkable recovery from extreme congestive failure after myocardial infarction illustrates the recuperative powers of a healthy heart with healthy coronary vessels—and also the value of digitalis in such a situation.

The antibiotic dosage must almost constitute a record for such a period of treatment. For example, 887 million units of penicillin were given intramuscularly in two months.

Idiopathic Hypercalcæmia with Subcutaneous Calcium Deposits following Pseudosclerema.—PHILIP R. CLAY, M.R.C.P. (for HELEN M. M. MACKAY, F.R.C.P., and WINIFRED F. YOUNG, M.D.).

C. H., female, birth weight 9 lb. 1 oz. Date of birth 26.1.55.

Antenatal history uneventful. *Mother did not take vitamin tablets supplied by clinic.* Some fœtal distress during the second stage of labour.

Past history.—Hæmolytic disease (Rh incompatibility) treated by exchange transfusion. Moderate jaundice subsided after five days. Further transfusion at 1 month 4 days. Patchy pseudosclerema over back and shoulders developed during first week.

Family history.—Fourth pregnancy, preceded by one miscarriage and the birth of two normal siblings.

History of present illness.—Feeding well on Cow and Gate full cream dried milk mixture, from second week of life until 1¼ months old when she weighed 10 lb. 2 oz. Thereafter anorexia with poor food intake for one month and vomiting for two days. No constipation. Weight loss to 9 lb. 8½ oz.

Vitamin D intake.—(1) Cow and Gate milk mixture supplied 750 units of vitamin D approx. (calculated from data supplied by Messrs. Cow and Gate Ltd.). (2) Cod-liver oil, 1 teaspoonful daily from age 1 month, taken poorly (800 units of vitamin D). Changed to: (3) Radiostoleum ℿ 7 b.d. (2,640 units of vitamin D) five days before admission.

Admitted 4.4.55 aged 2¼ months.

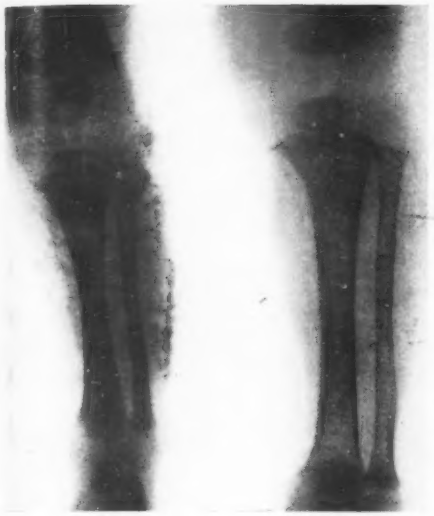
On examination.—Lethargic infant slightly dehydrated. Patches of pseudosclerema over back and shoulders. Nodular calcareous deposits in subcutaneous tissues of arms and legs without inflammation. No abnormalities of respiratory, cardiovascular or nervous systems.

Biochemical investigations.—On admission: Blood urea 120 mg./100 ml. Serum Na 155, K 3·8, Cl 118, CO_2 21 mEq./l. Urine acid; slight albumin, few leucocytes. *Following rehydration:* Blood urea 64 mg./100 ml. Serum Na 139, K 3·9, Cl 102 mEq./l. Serum Ca 17·4, phosphorus 5·3 mg./100 ml., Alkaline phosphatase 14·6 K.A. units. Urine (after eight hours thirsting) sp. gr. 1019.

X-ray examination (Dr. C. J. Hodson).—"(1) *Bones:* Well formed, bone age about correct. In metaphyses and epiphyses there is alternate zoning of more and less dense bone extending over a period which almost certainly began just before, at, or just after birth. Spine shows 'ghost' vertebræ, and skull shows increased density of the basal, frontal and occipital bones.

"(2) Extensive calcification in the *subcutaneous fat*, mainly of forearm and calves, less on upper thighs and upper arms with slight change over sacrum and shoulders." Fig. 1 shows appearances in the subcutaneous tissue of the leg at time of diagnosis compared with six months after treatment.

Treatment.—Tube feeding to restore and maintain hydration initially. From 20.4.55 low calcium milk (Locasol) substituted for Cow and Gate milk mixture to supply equivalent caloric intake. No vitamin A or D supplements.



14.4.55 21.10.55

FIG. 1.—X-ray appearances of subcutaneous calcium deposits in the leg at the onset and six months after the start of treatment.

ing difficulties were overcome slowly. However, without effective treatment, the disease

Progress.—After first week of treatment, there was clinical improvement for the following month with a gain of 1 lb. 5½ oz. in weight (10 lb. 3 oz. to 11 lb. 8½ oz.). Then exacerbation of feeding difficulties and vomiting until partial substitution of feed by full-cream Cow and Gate milk mixture. Thereafter rapidly improved and mixed feeding well tolerated. There was normal progress, mental and physical with normal skeletal growth and development.

Results of serial blood examinations and weight chart are shown in Fig. 2.

Present findings at 10 months. Normal serum calcium and blood urea levels. Residual subcutaneous calcium deposits. Physically and mentally well developed child.

Discussion.—This case appears to fall between the type described by Fanconi and others (1952) and the milder type described by Lightwood (1952*a*, *b*), since the bone changes are more common in the former.

The child responded well to the low calcium diet, but there was no dramatic change in general well-being. The feed-

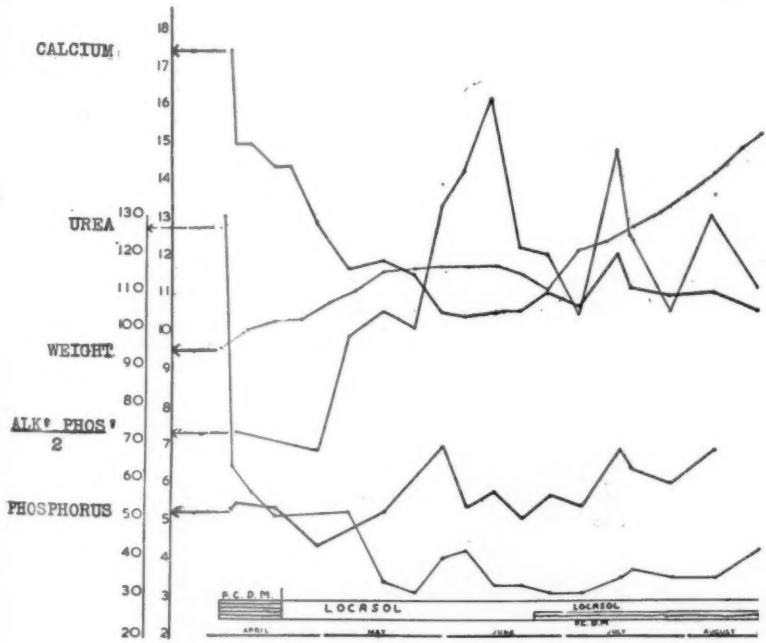


FIG. 2.—Progress from admission until four months after onset of treatment. Blood urea, serum calcium and phosphorus expressed in mg./100 ml. Alkaline phosphatase as $\frac{\text{K.A. units.}}{2}$

might have been expected to run a severe course with the possibility of residual renal damage and perhaps mental retardation.

The early onset of symptoms in this case is unusual, but in two cases described by Creery and Neill (1954), the symptoms began at six weeks, being diagnosed at 6 and 17 months respectively.

The extensive subcutaneous calcification is a feature not previously described. Calcium deposits are known to occur in areas of fat necrosis. These deposits did not occur, however, in the areas where pseudosclerema had been maximal.

Various theories have been put forward to explain the ætiology of this disease, including excessive vitamin D intake and hypersensitivity to vitamin D. This child had a low vitamin intake until the onset of symptoms and her mother took no vitamin supplements during pregnancy. Alkaline purgatives were not given. Hypersensitivity to vitamin D might be a factor in this case as suggested by several authors, most recently by Bonham-Carter *et al.* (1955) but excessive vitamin D intake is excluded by the history. The X-ray features are suggestive of a prenatal origin for the disease which is so far unexplained, but has been discussed by Russell and Young (1954) in describing two severely affected cases.

Acknowledgments.—I would like to thank Dr. Helen M. M. Mackay and Dr. W. F. Young for helpful criticism and permission to publish this case; Dr. B. Levin for the biochemical data and Dr. C. J. Hodson for his opinion on the X-ray findings.

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Dr. Thomas Stapleton: I think that several factors must be considered in the ætiology of this condition: the amount of vitamin D given (which cannot always easily be calculated), the individual variation in response to vitamin D, the calcium intake and the rate of growth of the subject. It is difficult to be certain from the radiological studies in this patient that abnormal changes had occurred before one month of age. An advantage in using calcium-free cereal (Glaxo) as well as Locasol, is the higher caloric value of the former.

Angioma Compressing Left Thorax.—CATHERINE A. NEILL, M.R.C.P. (for HELEN M. M. MACKAY, F.R.C.P., and V. A. J. SWAIN, F.R.C.S.).

S. G., female, aged 11 months (born 11.12.54 in Mothers Hospital). Premature infant. Birth weight 3 lb. 9 oz. Swelling in left infra-axillary region first noted at 4½ weeks of age; by 6½ weeks size of half-lemon extending anteriorly below clavicle; tense, slightly nodular, transilluminating very poorly. Lump above left scapula first noticed at 6½ weeks; rapidly

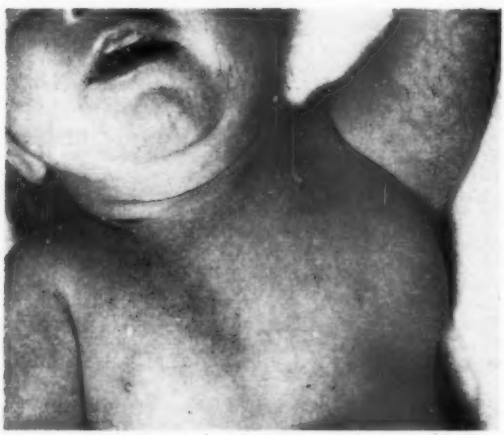
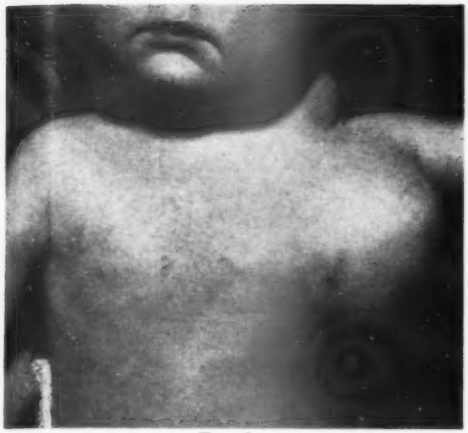


FIG. 1.—Aged 2 months. Showing swelling of left axilla.



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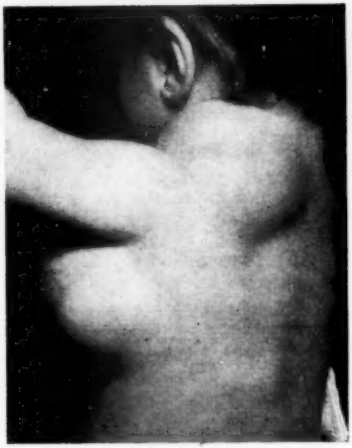

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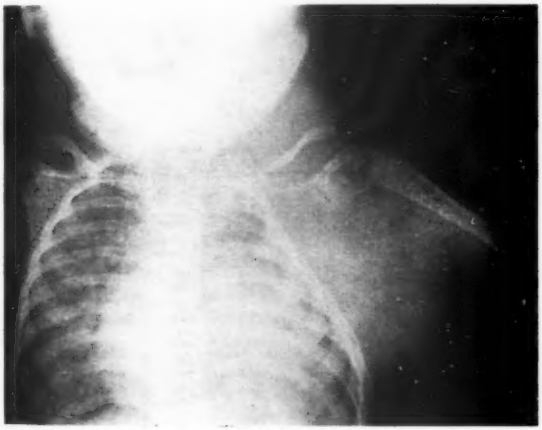

FIG. 4.

FIG. 2.—Aged 10½ months. Showing increased size of swelling in left axilla and in the neck.

FIG. 3.—Aged 10 months. Showing increased size of swelling in left axilla and neck.

FIG. 4.—X-ray aged 10 months. Showing size of mass, tracheal displacement and marked pressure on ribs.

enlarged over lower part of neck. Infant transferred to Queen Elizabeth Hospital for Children. By 2½ months veins over left anterior chest wall and capillaries over axillary swelling were prominent. Tracheal displacement to right and slight dyspnœa and recession noted at 5 months. Difficulty with taking solids, ? dysphagia, at 6 months. Otherwise asymptomatic apart from slow weight gain. By 6 months infra-axillary mass was size of a large orange. By 11 months of age swelling over left anterior chest wall had diminished and tracheal displacement was less. Other swellings same size as at 5 months of age (weight at birth, 3 lb. 9 oz.; 2 months, 8 lb. 1 oz.; 5 months, 11 lb. 3 oz.; 7 months, 12 lb. 11 oz.; 11 months, 15 lb. 4 oz.).

Family history.—Only child, healthy parents. No family history congenital abnormalities.

On examination (17.11.55).—Small vigorous baby. No dyspnœa. No recession. Trachea displaced to right. Dilated veins over left thorax. Soft cystic non-translucent mass in left infra-axillary region, extending over upper anterior chest wall, not pulsating. No bruit. Two similar masses left side of neck. Small button-sized nodule to left of mid-thoracic spine. Strawberry nævus below umbilicus. Fundi normal. Small umbilical hernia.

Investigations.—X-rays (Dr. C. J. Hodson): The soft tissue pattern of the masses suggests diffuse angiomata with very small blood or lymph spaces. The curved opacity overlying the first left rib and intercostal space may be intrathoracic, but this is unproven. Tracheal

displacement to right. Thinning distortion and sclerosis of the first left rib, and pressure deformity of left mandible and all left ribs. Slight hypertrophy of the scapula, humerus and clavicle. No recent change.

Bronchoscopy, June 1955 (Mr. J. R. Belcher): No evidence of bronchial or œsophageal obstruction. Surgery not advised.

Aspiration, November 1955 (Mr. V. A. J. Swain): No fluid obtained from lower rounded part of axillary mass. Hb 90%. Platelets 226,000.

Discussion.—Dr. White Franklin suggested that this was a hæmangio-endothelioma, and recommended platelet count and biopsy. Platelet count 226,000. Biopsy not undertaken since in the absence of increasing pressure symptoms surgery was considered to be contra-indicated by Mr. J. R. Belcher, and radiotherapy at this young age would produce severe stunting of thoracic growth (Dr. Gwen Hilton, University College Hospital).

POSTSCRIPT (August 1956).—When last seen all the masses had strikingly decreased in size.—H. M. M. M.

Swelling Right Parotid Gland.—TREVOR P. MANN, M.D., D.C.H.

Infant R. D., male, aged 4 months. Birth weight 6 lb. 15 oz. Normal delivery. Breast fed. Painless swelling right parotid region first noticed at age of 7 weeks. Baby otherwise healthy. Examination at this time revealed a firm, perhaps slightly tender, tumour occupying position of right parotid gland. No apparent change in size when feeding at breast or after orange juice. No signs of inflammation. Mouth healthy. Initial diagnosis—Caffey's disease, but no bony changes found.

Infant has subsequently thrived and remained in perfect health. Swelling has become more pronounced (Fig. 1) but size stationary over last month. No change in size or consistency with feeding but mother believes tumour sometimes enlarges and hardens on crying. Examination shows that swelling is now more obviously in the exact position of the parotid gland. It is fluctuant and definitely not tender. No discoloration of tissues over mass. Parotid duct orifice normal; no stone palpable. Sialogram unsuccessfully attempted. No change in swelling on crying.

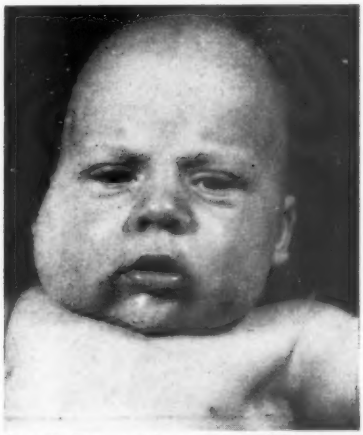

FIG. 1.—Infant R. D., aged 4 months. Right parotid swelling.

Differential diagnosis.—Hæmangioma, lymphangioma and lipoma were considered originally but not now favoured. Partial duct obstruction seems most likely cause of parotid swelling.

POSTSCRIPT (August 1956).—Aged 1 year. Beginning of April 1956, swelling disappeared. First week of May it reappeared, but only for a few days during a coryzal attack. It has not been observed since.

Unilateral Internal Ophthalmoplegia Due to Chickenpox.—THOMAS E. OPPE, M.B., M.R.C.P. (for THOMAS STAPLETON, D.M.).

R. C., male, aged 8.

Seen in October 1953 three weeks after the onset of typical mild chickenpox. Five days following the initial eruption, his right eye had become bloodshot without pain or photophobia. When the redness subsided it was noticed that his right pupil was dilated. At no time during this illness were symptoms or signs of meningo-encephalitis apparent.

On examination.—Apart from the subsiding lesions of varicella, the only abnormalities were found in the right eye. The pupil was fixed and dilated, reacting neither to light nor to convergence. Accommodation was probably paralysed. Light shone into the right eye produced a brisk consensual contraction of the left pupil. There was no proptosis and the external ocular movements were normal.

Essentially the condition has remained unchanged, although the right pupil has diminished in size slightly and become asymmetrical.

Comment.—It is presumed that the lesion described is due to involvement of the ciliary ganglion by the chickenpox virus. As an isolated occurrence during varicella it is extremely rare. Ocular paralyses of this type are sometimes seen as part of chickenpox meningo-encephalitis, but these usually recover (Underwood, 1935; Appelbaum *et al.*, 1953). Internal ophthalmoplegia has been reported as a complication of herpes zoster ophthalmicus (Hohnberg, 1951).

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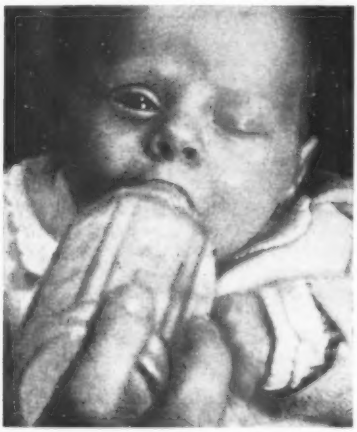

FIG. 1.—Jaw-winking of right eye.

Jaw-winking (Marcus Gunn Phenomenon).—D. MORRIS, M.R.C.P.

P. B., male, born 3.10.55. Upward movements of right upper eyelid accompany sucking. No apparent ptosis. Baby is otherwise quite fit and well. Mother, primipara of 20, has always had "heavy lids", slight ptosis of left eyelid. No family history.

A cine-film of this condition was shown (*see* Fig. 1).

[*This November meeting to be continued in September "Proceedings".*]

[*January* 27, 1956]

DISCUSSION ON THE MANAGEMENT OF ASPHYXIA IN THE NEWBORN

Mr. J. B. Blaikley:

Management of Asphyxia Neonatorum

It is difficult I think to assess the risks of asphyxia neonatorum, for clearly the central nervous system of an unborn child is capable of complete recovery from quite a long period of complete anoxia. I have myself resuscitated a baby delivered 45 minutes after prolapse of the cord with complete cessation of placental circulation; the baby died within 24 hours. I have too, in Dublin, been shown a 12-year-old boy delivered 45 minutes after internal version with complete rupture of the umbilical cord; he had paralysis and wasting of much of his musculature and was aphasic, but could play the piano with his big toes (his fingers were useless), and he appeared to understand conversation. I have resuscitated with difficulty an almost pulseless baby, full of inhaled meconium and as badly asphyxiated as I have seen, who subsequently gained an exhibition to Cambridge. Forty-five minutes complete anoxia is too long, but at what shorter period does permanent damage occur? Further, does prolonged hypoxia from difficult labour or from placental insufficiency due to infarction or other causes produce damage? On top of prolonged hypoxia, quite a short period of acute anoxia must have ill-effects. I think at present we tend to exaggerate the risks of short periods of oxygen-lack but none the less we are right in trying to avoid unnecessary prolongation of anoxia.

The great majority of anoxic babies respond very quickly to the standard simple measures; clearing the airway of liquor and mucus, and if necessary cutaneous stimulation. But the flaccid pale baby that does not spontaneously breathe quite quickly, calls for more vigorous measures without delay.

The urgent need is to get oxygen to the medulla, and clearly the method of resuscitation used should be generally applicable and therefore simple. In 1935 Gibberd and I described a method of tracheal intubation and insufflation with oxygen, and at that time we found both Flagg and De Lee in America had done so before us. The apparatus consists of a silk-web Magill catheter connected to a rubber bag of 3–4 litres capacity which, in turn, is connected to an oxygen cylinder. Between the bag and the catheter a T-piece is inserted for the attachment of a manometer. I have used this method ever since and I still think it is the most satisfactory way of dealing with a serious case. The method is quick and with a little practice not difficult. I personally have always passed the catheter by touch; the left index finger passed into the pharynx feels the two arytenoids and guides the catheter into the larynx, but most people prefer to use a direct-vision laryngoscope. I normally use a No. 3 catheter and blow oxygen through it at a pressure of 30–35 cm. water. The bag acts as a reservoir and buffer, so any sudden rise of pressure and consequent injury to the lungs is avoided. Experimental insufflation of fresh stillborn babies shows that these pressures do not expand atelectatic lung, but only ventilate the bronchi and trachea, while higher pressures cause emphysema of the lung margins and even rupture of the dilated alveoli. I have never caused rupture in the course of resuscitation and have successfully resuscitated all babies with evidence of heart action except some shown *post mortem* to have intracranial hæmorrhage. It is surprising how quickly the colour improves, and I have been interested, too, to find that the mere passage of the catheter between the vocal cords is a very powerful stimulus and will often initiate respiration.

The pressure of gas in the lungs is about half that in the bag, so Gibberd and I found, and provided there is free return of oxygen through the glottis, a pressure of 35 cm. of water in the bag is quite safe. The presence of a rubber bag between the cylinder and the catheter is an essential safety measure. Firm pressure with the hand on the nearly full bag produces just the right pressure. I would like to emphasize that it is not possible to expand the alveoli themselves by insufflation, and that this can only be done by spontaneous inspiration and expiration.

I frequently use the catheter to aspirate liquor and debris from the trachea and bronchi before proceeding to insufflation.

Of recent years treatment of asphyxia neonatorum with intragastric oxygen has become popular. It was started in Scandinavia, and in this country the late Dr. H. Waller took it up enthusiastically. I have no personal experience, but from talking to my registrars it would seem that the method is not as efficacious as intratracheal oxygen in serious cases, but will tide over a difficult period till a doctor comes to the help of a midwife. Its advantage is the ease with which a double catheter can be passed into the stomach, and so it is readily passed by those unskilled in tracheal catheterization. There is some danger in passing a tube that is rigid into the stomach, it should be quite soft.

A good deal of difficulty in the early stages of respiration could be avoided if all babies were held upside down immediately after delivery, and were then transferred if not breathing well to an inclined table, head down and when possible half on the face, so that liquor tends to run away from the larynx and pharynx as it pours from the trachea and perhaps œsophagus too. The importance of postural drainage is gradually being appreciated, and I think much subsequent respiratory difficulty can be avoided if this is instituted before the baby takes its first real breath. Before the thorax is born it cannot inspire much, but as soon as it is born the baby can practically drown from inspiration of liquor. Cæsarean babies are especially liable to have liquor in their mouths and upper air passages at birth and they, in particular, need postural drainage, often for some hours.

I am not competent to say whether routine aspiration of the stomach is to be advocated as I have not used the procedure. Lethidrone I never use. I gather there is a good deal of variability in its action and I have become so confident in the use of the intratracheal catheter in severe asphyxia, and resuscitation is so prompt by this method that I find no need for this drug.

Severe asphyxia neonatorum can often be avoided by the obstetrician if he notices the early signs of fœtal distress *in utero* and if he avoids delay in the second stage when it can develop very rapidly. Oxygen administered to the mother through a B.L.B. mask will improve the fœtal heart-rate for an hour or two if there must be delay before applying forceps.

It is nowadays customary to put a few inches of rubber tube on the end of a mucus catheter. I believe this is wrong, the rubber is difficult to control whereas the curved metal tip can be placed accurately on to the glottis so that mucus and thick meconium can be

cleared from this important region. I have seen a baby take a few breaths and then when all seemed well suddenly stop breathing and go pale due to mucus being inhaled into the larynx with an immediate reflex collapse. A mucus catheter properly used will clear the airway and usually re-establish respiration, but it may be necessary to pass a catheter into the trachea before the alarming collapse is relieved.

Intratracheal insufflation with oxygen is the method of choice in the treatment of severe asphyxia neonatorum; if it is not severe simple measures and the inhalation of oxygen through a close-fitting mask is enough.

REFERENCE

BLAIKLEY, J. B., and GIBBERD, G. F. (1935) *Lancet*, i, 736.

Dr. G. F. Abercrombie:

I shall try to indicate what appear to be the best and simplest measures, which a general practitioner can undertake, both in prevention and in treatment. Let it be remembered that he does not possess a Phrenic Stimulator, or a Positive Pressure Oxygen Air Lock, or even an Emergency positive pressure patient-cycled Respirator. Let us give him a mucus catheter, a cylinder of oxygen and a hypodermic syringe, and see what can be done.

Blue asphyxia, which is by far the commoner, seldom gives rise to real anxiety. A clear airway and a little patience will nearly always be rewarded by the spontaneous establishment of satisfactory respiration, and by the change of colour from blue to pink. If this fails, then certainly a respiratory stimulant, as described later, should be injected.

White asphyxia, on the other hand, is unmistakable and almost certainly the climax of a long, tedious and difficult confinement. The infant when born is ashy-white, and it is limp, toneless, all the muscles completely relaxed. It is the picture of profound shock; in a word, it is "out". The heart can just be felt to beat at longish intervals, and at the end of five minutes, there may be a single, sickly, gasping sigh. The placenta is still in the uterus, and the attendant is gowned, gloved and masked, and must remain so, for a post-partum hæmorrhage may occur at any moment. What is to be done?

If the conviction is borne in upon one towards the end of labour that vaginal delivery may prove to be difficult at least one will summon a highly-skilled anæsthetist, for the oxygen that he will incorporate in his choice of anæsthetic agents may well be life-saving. If the mother has received narcotic drugs of the morphine group, and particularly if one is compelled to deliver within two or three hours of the latest hypodermic injection, a full dose of Nalorphine should be given intravenously. Episiotomy is essential, and the delivery should be conducted with the utmost gentleness.

Should the umbilical cord be divided at once or not? It appears that one-quarter of the human fœtal blood is in the placental circulation at the end of pregnancy. When pulsation ceases in the umbilical arteries, contraction of the uterus forces blood into the circulation of the infant through the umbilical vein. "Deprivation of placental blood, by clamping the umbilical cord immediately upon delivery, is equivalent to submitting the infant to a hæmorrhage at birth" (Windle, 1950). It will be best, therefore, not to divide the cord, until the uterus has expressed the placenta.

Unless the cord is very long, it will not be possible to put the infant in a warm bath. This is just as well, for the right course is to wrap it in a hot towel and hold it with the head low—low enough for mucus and liquor amnii to drain from the nose and mouth. This process may need to be assisted by a mucus catheter, and it is probable that, if necessary, the highly skilled anæsthetist can intubate the larynx by direct vision and deliver oxygen under pressure when the airway is clear.

Short of that, I should administer oxygen by the method described by Knowles (1952) who leads it in a gentle stream through a rubber catheter to the child's mouth. The lips are pursed around the catheter by the thumb and fingers of one hand, while the infant's nostrils are closed by the other. "At once", he says "the chest will be seen to expand and both hands then relax to allow the chest to deflate. The inflation and deflation of the lungs can be rhythmically continued as long as necessary." This, to me, sounds more satisfactory than the giving of oxygen into the stomach through polythene tubes.

Finally, there is the question whether to inject into the infant a respiratory stimulant—some form of camphor—and, if so, how. This procedure receives little support from the experts, who suggest that so-called respiratory stimulants are of little value, and that general practitioners should not panic from one manœuvre to another. On the other hand, Leak (1953), after commenting on the wonderful ingenuity that is being shown in overcoming asphyxia by methods far out of the reach of the general practitioner, whole-heartedly

advocates the injection of leptazol or Cardiazol ephedrine direct into the ventricle of the heart. "Within a few seconds", he says, "it takes the infant from the non-breathing or occasional gasping stage to full respiration and vigorous crying." Now I must confess that, if an occasion arose when I felt I ought to inject something into the infant, I should much prefer not to fiddle about with the umbilical vein, and I should never feel that I had done all I might, unless and until I had acted as Leak advises.

Therefore, to sum up, leave the cord alone, keep the child warm, handle it gently, clear the airway, administer oxygen, and if a convulsant still seems essential, it should be a full dose direct into the ventricular cavity.

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LEAK, W. N. (1953) *Brit. med. J.*, ii, 510, 887.
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Dr. Hugh Jolly, referring to Dr. Abercrombie's list of equipment to be carried by the general practitioner for the treatment of asphyxia neonatorum, felt it was an omission not to have included means for the administration of gastric oxygen. This equipment, consisting of two catheters and a "sparklet" oxygen bulb was now carried by midwives in Plymouth and he thought that all those practising midwifery should do the same.

Dr. D. MacCarthy: In reference to Knowles' method of administering oxygen described by Dr. Abercrombie, I think that some oxygen is likely to enter the stomach; just as in the old method of mouth to mouth respiration air entered the stomach. The resuscitating effect can therefore be possibly due as much to intragastric oxygen as to bronchial insufflation.

Dr. D. Hilson: In my view there is a dangerous school of pædiatricians who take the attitude that the less you do in resuscitation, the better. An attitude of masterly inactivity leaves one smug but ineffective and in this field reminiscent of the earlier surgeons who declined to act on Murphy's advice for early operation in appendicitis on the grounds that most did as well if they were left alone. It is true that meddlesome over-activity is dangerous but the only way to appreciate the limitations is by constant attendance in the labour ward.

Phrenic nerve stimulator.—This instrument has not been given adequate praise in the literature. Properly used, it is the simplest aid for resuscitating the child in the flaccid state. For proper use one must bear in mind the following requirements:

The tongue must be cleared off the palate, to which it often clings. The airways must be cleared or the violent contraction of the diaphragm will force liquor into the deep respiratory passages. The dial on the instrument must be set at full strength, because the more anoxic the child, the less it responds, but having responded one can utilize very much lower current strength. The negative electrode under the back should be adequately padded and adequately wetted. Most important of all is the position at which the electrode will find the phrenic nerve; it is most easily found by tucking the electrode in below the lateral angle of attachment of the sternomastoid to the clavicle. This is much easier to find in the flaccid newborn than the posterior margin of the sternomastoid where the phrenic nerve emerges. A hypodermic needle can be inserted through the wire and through the lateral attachment of the sternomastoid muscle and left in situ so that the baby can be nursed in oxygen and warmth for prolonged periods. The nursing staff turn the dial down intermittently and if the child does not take over respiratory control they increase the strength of the current. I have had such infants on prolonged stimulation for over thirty hours. Many of them are no more or less than "heart-lung preparations".

The instrument has also been used to re-start the heart after arrest, by plunging a needle into the ventricle and applying the electrode directly to the hub of the needle. This has resulted on three occasions in the heart beating for 30, 35 and 40 minutes respectively after the heart beat had ceased. In the second case stimulation was not commenced until 8 minutes after cardiac arrest.

Properly utilized, one hopes that this instrument will provide another means of prolonging life.

Intratracheal oxygen.—This is an extremely useful measure and if the heart is beating there is never any doubt that the baby will flush pink if the oxygen goes in at a sufficient pressure to reach the lung tissues.

Having utilized it on many occasions I feel that, although one must be cautious of the pressures, it is rare for rupture of the lung to occur, as excessive pressure of oxygen can always escape back up past the catheter. Most of the post-mortem lungs that are found

ruptured have probably been ruptured by intratracheal oxygen administered after death of the baby. Excessive oxygen should be suspected when the baby is pink but not breathing and one only has to pinch off the catheter and allow the baby to go blue to see whether it will make its own respiratory efforts and justify removal of the intratracheal oxygen-carrying catheter.

Eaves' rocking method.—This is very useful as a temporary measure of resuscitation but its danger lies in the fact that so many babies have torn tentoriæ and movement of the head is likely to encourage bleeding. I practise it holding the baby's head stationary, or resting its head on a table edge and raising and lowering the feet so that the body moves through 40 degrees either side of the horizontal.

Sternal traction in the premature baby with gross indrawing of the sternum.—This is a life-saving procedure, particularly when the baby is having cyanotic attacks.

Dr. B. W. Powell: It is interesting to remember that Barcroft compared the process of being born to going up into a high mountain whereas Clement Smith likens it to descent into a valley. Perhaps this illustrates the different viewpoints of physiologist and clinician.

Having had experience of various elaborate forms of apparatus and methods of resuscitation, for practical purposes a provincial pædiatrician comes back to simpler methods which can be readily taught and applied.

Gastric oxygen given through a fine polythene tube certainly seems an effective way of preventing or lessening cyanosis during the first few hours of life. I have never known it do any harm and have often seen it do good. Combined with other simple methods it may tide the infant over a period of dangerous anoxia.

Dr. David Morris: I first came across human hibernation, artificially induced in premature babies, in Paris when visiting l'École de Puericulture. Dr. Rossier and Professor le Long had, for some time, been treating ill premature infants with birth injury or hyaline membrane by chlorpromazine. The babies reacted to the lowered external temperature in their incubators and were kept between 85 and 90° F. for two to three days.

Concerning intragastric oxygen, it was the experience of the midwives at the British Hospital for Mothers and Babies that made us decide to continue its use, but obviously more knowledge is needed as to how it works. A detailed study is being carried out at present, and already interesting information is coming to light. Why did some babies who responded to this method not go pink before they started to breathe? If the blood oxygenation improves by absorption of oxygen from the alimentary tract, we would expect the baby to become pink before the respiratory centre is stimulated to work.

Dr. J. J. Kempton: In Reading we have very largely limited measures of resuscitation to simple procedures which can be carried out by trained nurses. These consist in the maintenance of a clear upper airway using a bulb sucker, postural drainage (with sometimes steep posturing), and the administration of oxygen by tube and funnel, and by gastric catheters.

One further measure adopted during the last two years has seemed of great value in a few cases, in which a severe degree of inspiratory collapse of the anterior chest wall was present. This is sternal traction as described by Love and Tillery (1953). A small towel clip is attached to the fascia over the lower end of the sternum and a length of elastic joins this to a letter clip on the edge of the cot in such a manner as to exert a steady tension. The occasions for this are very few, but it has at times seemed a life-saving measure.

Our autopsy results seem to show that when simple measures of resuscitation fail in a full-term infant, either cerebral hæmorrhage or some congenital abnormality is almost invariably found.

REFERENCE

LOVE, W. G., and TILLERY, B. (1953) *Amer. J. Dis. Child.*, **86**, 423.

Dr. B. M. Laurance: I feel that the value of aspiration of the newborn's stomach has been insufficiently stressed in this discussion. Babies born by vertex deliveries benefit by pressure on the abdomen after the head and chest are born so that the stomach contents are emptied. This is not the case in babies born by Cæsarean section or by breech delivery and I have frequently aspirated as much as 20 ml. of liquor amnii from the stomachs of babies born in this way. The risk of their inhaling this material is thereby greatly lessened.

Mr. Wilfrid Mills: The object of delivering oxygen to the vital centres of the newborn baby can be achieved in many ways, either by stimulating respiration or by injecting oxygen artificially. When a supply of oxygen is not available the most powerful respiratory stimulation can be given by the injection of one of the convulsant drugs. I prefer the use of Coramine (nikethamide) in 0·5 ml. dosage into the umbilical vein. This will produce respiration in any baby whose heart is beating unless there be gross cerebral hæmorrhage. The only danger of this method is the production of gluteal necrosis if by chance the injection be made into the umbilical artery.

Dr. Norman F. Elliott Burrows: Coramine in small doses (i.e. under 0·5 c.c. at a time) injected intravenously extremely slowly is of great value in resuscitating asphyxiated newborn babies, but I have caused convulsions in a baby by injecting 1 c.c. of Coramine fairly rapidly.

Dr. A. G. Doughty: Intragastric insufflation of oxygen is likely to be particularly efficacious in the premature infant in whom the poorly-developed gastric mucosa offers less resistance to the passage of oxygen than in the full-term child. It is in the premature infant that the small size and fragility of the glottis and trachea make attempts at laryngeal intubation undesirable. For these reasons intragastric oxygen is indicated in the premature and endotracheal oxygen in the full-term infant.

Dr. Helen Mackay: Proof of the value of any method of treatment is difficult to come by, and impressions vary widely. Many forms of treatment have been advocated in this discussion, from "severe shocks" by way of stimulation of the phrenic nerve, to chilling of the infant to 91° F. so that his tissues can do with the minimum of oxygen. Surely one's object with an asphyxiated neonate is to get him to breathe, and to keep him breathing normally, so that the tissues are properly oxygenated, not to try to make his tissues do with the minimum of oxygen. The chilled baby's breathing is shallow, and his vitality is minimal. Is he more likely to stop breathing for good if we chill him or if we keep him warm? I shall continue to try to maintain my newborn infants' temperatures at around 98·4° F.

Dr. Shila Ransom: In response to expressions of doubt on the matter of absorption of oxygen from the stomach I am glad to say that I have seen infants grow pink under administration of gastric oxygen before they showed any obvious signs of breathing. A particular merit of this method of treatment is that it can be used by the only person who is always immediately available—the midwife.

Dr. Trevor P. Mann: The application of induced hypothermia to the management of neonatal asphyxia seems rational. We have found that the progress in the early days of life of certain very small premature infants has been smoother when their body temperatures have been allowed to stabilize, in a warm environment (80–90° F.), well below the generally recommended level of 96–97° F. By allowing the temperature to fall thus, the baby's metabolism is set at a correspondingly lower level and in consequence oxygen requirements are lessened. Cyanotic attacks appear less liable to occur and even more important oxygen therapy with its attendant dangers usually becomes unnecessary. Needless to say, such treatment should only be used in hospital and our experience in recent winters in Brighton with babies suffering from neonatal cold injury following accidental cold exposure in the home suggests that it is dangerous to allow the temperature of the newborn to fall below 90° F.

For some years now (usually during spells of severe weather) we have been seeing newly-born infants suffering from profound hypothermia consequent upon chilling in cold homes. Although at first sight these babies generally have a misleading appearance of well-being, many of them rapidly deteriorate and die on re-warming. It would appear that irreversible damage to vital structures, particularly small blood vessels, may quickly follow a reduction of the infant's body temperature to below 90° F. Biochemical, metabolic and circulatory disturbances, difficult to reverse, may also explain unexpected re-warming deaths. Evidence derived from this source suggests that the application of induced hypothermia is not without danger in the very young. The baby's temperature must be watched carefully during cooling and in my opinion, it should not be allowed to fall into the eighties, otherwise cold injury may ensue.